OMB No. 0990-0115

Electronic Request for Proposal

SECTION A – SOLICITATION/CONTRACT FORM

OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE CMB WEBSITE http://www.niaid.nih.gov/contract/default.htm FOR ANY POSSIBLE SOLICITATION AMENDMENTS THAT MAY BE ISSUED. NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS WILL BE PROVIDED BY THIS OFFICE.

Purchase Authority: Public Law 92-218, as amended.
NOTE: The issuance of this solicitation does not commit the government to an award.

RFP Number:	***Just In Time:***	Small Bus. Set-Aside [ ]Yes [X]No 8(a) Set-Aside [ ]Yes [X]No NAICS Code: 541710 Size Standard: 500 employees or less	***Level of Effort:*** [ ] Yes [X] No ***Total Effort:*** [ ]
NIH-NIAID-DAIT-03-31	[ ] Yes [X] No		

TITLE: **Immune Epitope Database and Analysis Program**

Issue Date: August 29, 2002	***Due Date: November 26, 2002*** ***Time:*** **4:00 PM, EST**	***Technical Proposal Page Limits:*** [X] Yes *(see "How to Prepare and Submit Electronic Proposals")* [ ] No

ISSUED BY:
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[X] ***We reserve the right to make awards without discussion.***

NO. OF AWARDS:	***PERIOD OF PERFORMANCE:***
[X] Only 1 Award [ ] Multiple Awards	5 years beginning on or about 09/01/2003 2 one-year options

Offers will be valid for 120 days unless a different period is specified by the Offeror on the form entitled "Proposal Summary and Data Record, NIH-2043" (See SECTION J - Attachments)

The Official Point of Receipt for the purpose of determining timely delivery is the Contract Management Branch as stated above. The paper copy with original signatures is the official copy for recording timely receipt. If the paper copy of your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with HHSAR 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation. FACSIMILE SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.

POINT OF CONTACT **-- Suzanne L. Dawkins** ***--COLLECT CALLS WILL NOT BE ACCEPTED-***

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Background

Immune Epitope Database and Analysis Program

DAIT-03-31

Introduction

The National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) supports research related to basic understanding of immune responses leading to the development of vaccines and novel therapeutic agents for the prevention and treatment of infectious and immune-mediated diseases, and improvements in public health. This includes support of various reagent facilities, repositories, and databases that provide resources for biomedical researchers. As a part of the research program to improve defense against biological terrorism and emerging/re-emerging infectious diseases, the NIAID seeks to establish a comprehensive database of molecular structures recognized by the immune system. These structures, termed epitopes, attach with lock and key precision to receptors of the immune system, namely B cell antibodies and T cell receptors. The immune system is able to respond to an enormous number of epitopes. An unlimited number of antibody epitopes and 5×10^{11} T cell epitopes are estimated to exist. The number of known epitopes currently available for incorporation into a database is many times smaller, but new epitopes are continually being discovered and large numbers can be identified by current techniques. Creation of a central standardized database, with a priority for epitopes associated with bioterrorism agents and emerging/re-emerging infectious diseases, will greatly facilitate utilization, for biodefense purposes, of the growing bank of antibody and T cell epitope information. In addition to enhancing research aimed at understanding epitope generation and immune recognition, creation of an Immune Epitope Database and accompanying Analysis Resource will expedite the development of improved vaccines and immunotherapeutic agents. The purpose of the project is two-fold:

A. The primary purpose of this project is to design, develop, populate, and maintain a publicly accessible, comprehensive Immune Epitope Database containing linear and conformational antibody epitopes and T cell epitopes composed of MHC-binding peptides and ligands (e.g., carbohydrates, lipids, and modified peptides) with a priority for epitopes associated with NIAID category A-C potential bioterrorism pathogens and their toxins (listed at http://www.niaid.nih.gov/dmid/biodefense/bandc_priority.htm). The Immune Epitope Database will be freely accessible to the scientific community via an Internet website.

B. An Analysis Resource will be developed and maintained by the Contractor, which will include online access to: (1) tools to help researchers locate and analyze information contained in the Immune Epitope Database; (2) other relevant databases and related information; (3) data mining algorithms, mathematical models, and other sophisticated analytical tools to help researchers identify novel antibody and T cell epitopes from genome or protein sequence information, predict the immunogenicity and/or antigenicity of epitopes, and predict host immune responses to particular epitopes; and (4) a quarterly newsletter for the scientific community and an annual compendium of data in the Immune Epitope Database and analytical tools (as described below) provided at the web site during the previous year. The Contractor will develop improved algorithms, models, and other analytical tools for use in discovering new knowledge from the database. All of the information contained within the Analysis Resource, including analysis tools and algorithms, will be made freely available to the scientific community.

Background

The main function of the immune system is to protect the host from infection by pathogenic organisms, such as bacteria, viruses, fungi, and parasites. Two arms of the immune system, innate and adaptive, work in concert to provide surveillance for foreign invaders. Innate immunity is characterized by rapid responses within minutes or hours of infection due to recognition of molecular patterns found widely on microbes but absent in higher organisms. Adaptive immunity is characterized by more specific responses generated by B and T cells that result in long-term protection against antigens (molecules that appear abnormal or foreign to the host). The adaptive immune system causes activated B and T cells to expand greatly in number in response to antigens and to persist as memory cells that are immediately ready to rid the host of these foreign invaders upon re-exposure to the same antigens. The antigen specificity of the adaptive immune system depends upon B and T cell receptor molecules, which bind strongly to epitopes of target pathogen molecules.

Antibody epitopes (also called B cell epitopes) consist of molecular structures on the surface of foreign molecules that are directly contacted by a particular antibody. Antibodies recognize two types of epitopes, linear and conformational. Linear epitopes are formed by a continuous sequence of amino acids in a protein, whereas conformational epitopes are composed of amino acids or components associated with carbohydrates or lipids that are discontinuous in the primary sequence but are

brought together during molecule folding. Generally, antibodies raised against whole proteins or non-protein molecules recognize conformational epitopes and those raised against molecular fragments recognize linear epitopes. There are exceptions to these observations, thus making it possible to use antigen fragments or synthetic molecules in vaccines to induce antibodies against the native molecule.

T cell epitopes consist of short molecule fragments held precisely in a pocket-like groove of MHC class I, class II, non-classical, and MHC-related molecules. MHC molecules are polymorphic proteins that bind to molecular entities (ligands) residing within different kinds of cells and then bring them to the cell surface so that T cells can recognize them. Most ligands are protein fragments, termed peptides, derived from proteolytic cleavage of foreign or self antigens. However, some ligands are derived from cleavage of carbohydrates or lipids. The MHC-ligand complex found on the surface of antigen-presenting cells (APCs) forms the T cell epitope. The three-dimensional structures of MHC-ligand complexes show intimate contact between the backbone/side chain amino acids of a peptide ligand and the variable region amino acids of the MHC molecule. Therefore, each distinct MHC molecule has its own rules for ligand binding, but generally can bind a large number of different ligands derived from foreign or self proteins. Given that there are at least 1500 different MHC alleles in the human population and an enormous number of possible ligands derived from self or foreign proteins, the number of potential MHC-ligand complexes is very large. For the purpose of this contract solicitation, the term "T cell epitope" will include all ligands (derived from proteins, carbohydrates, or lipids) bound to any member of the family of MHC and MHC-related molecules, thus encompassing all MHC-ligand complexes that are known to, or have the potential to, trigger T cell responses.

MHC-related molecules and non-classical MHC molecules likely present antigen to various types of T cells. There are more than 50 non-classical MHC genes identified in mice and more than 20 in humans, and an increasing number of MHC-related molecules continue to be identified. While the natural ligands for most of these molecules are not defined, there is considerable evidence suggesting that the MHC-related and non-classical MHC molecules bind a variety of antigens. For example, the mouse non-classical M3 molecule binds formylated peptides, allowing M3 molecules to present degraded bacterial products to T cells, whereas the mouse Qa-1 molecule predominately binds signal peptides from MHC class I molecules. The class I MHC-related molecule, CD1, seems to specialize in presentation of lipid/glycolipid molecules. Several recent research studies have shown that non-classical MHC and MHC-related molecules present chemically distinct ligands to a variety of T cells and are critical for generating protective immune responses.

The effectiveness of immune responses is related to the diverse functions of B and T cells as well as to antigen specificity. With respect to diversity, B cells secrete antibodies with different functions and T cells differentiate into groups that lyse infected target cells (cytotoxic T cells), secrete inflammatory cytokines (Th1 cells), or promote powerful antibody responses (Th2 cells). Knowledge of antigen specificity is also very important; not all parts of an antigen can serve as epitopes for a variety of reasons, including antigen structure, antigen processing and presentation, and B and T cell recognition capabilities. Actual epitopes are currently difficult to predict and epitope identification will be greatly enhanced by better information on the epitopes associated with antibodies and the entire family of MHC and MHC-related molecules. Such knowledge will expedite the development of new therapies to prevent and treat infection, and prevent organ and tissue transplant rejection, and autoimmune and allergic disorders.

Need for an Immune Epitope Database and Analysis Resource

On June 5, 2001, the NIAID convened an expert panel of immunologists and bioinformaticians to advise on the state-of-the-art and the scientific needs for a MHC-ligand T cell epitope database (See Section N for the Executive Summary MHC Peptide Minutes and the Planning Meeting Summary: MHC Peptide Database). The panel concluded that there is a strong need for a comprehensive MHC-ligand database as a central resource to consolidate efforts and to provide ready access to basic information and analysis/prediction tools. In addition, information on particular antibody epitopes associated with different bioterrorism pathogens and their toxins will facilitate the development of antibodies for passive treatments and new vaccines for prevention of infection.

Although several MHC-ligand databases currently exist, the proposed Immune Epitope Database will have a broader scope and will be routinely updated and curated. The following is a partial list of existing web-based MHC-ligand databases and predictive algorithms:

BIMAS (Bioinformatics and Molecular Analysis Section): Kenneth C. Parker
http://bimas.dcrt.nih.gov/molbio/hla_bind/index_using_only_9_and_10_mers_old_asof_7_22_96.html

EpiVax: Anne De Groot
http://www.EpiVax.com/

ESI (Epitope Identification System): Epimmune
http://www.epimmune.com

FIMM: Vladimir Brusic
http://sdmc.krdl.org.sg:8080/fimm/ and
http://wehih.wehi.edu.au/mhcpep/

HIV Molecular Immunology Database: Los Alamos National Laboratory, Bette Korber et.al.
http://hiv-web.lanl.gov/immunology/index.html

HLA Ligand/Motif Online Database System: William Hildebrand
http://hlaligand.ouhsc.edu/LigandDB/servlet/GenerateFormServlet?form_type=index

MAPPP (MHC-I Antigenic Peptide Processing Prediction): Peter Michael Kloetzel
http://www.mpiib-berlin.mpg.de/MAPPP/

NetChop, Center for Biological Sequence Analysis: Soren Brunak
http://www.cbs.dtu.dk/services/NetChop/

PAProC (Prediction Algorithm for Proteasomal Cleavages): Hans-Jorg Schild
http://www.paproc.de/

SYFPEITHI: Hans-Georg Rammensee
http://syfpeithi.de

Vaccinome's TEPITOPE - 2000: Jürgen Hammer
http://www.tepitope.com/

In summary, development and maintenance of a comprehensive Immune Epitope Database and Analysis Resource will:

1) Facilitate the identification of antibody and T cell epitopes associated with bioterrorism agents and other infectious organisms for their use as targets for passive immunotherapy and vaccine candidates.

2) Foster the development of more robust algorithms, mathematical models, and other predictive tools for identifying novel antibody and T cell epitopes from genome or protein sequence information and predicting host responses to specific epitopes.

3) Provide a central source of data on linear and conformational antibody epitopes.

4) Provide a central source of data on ligand binding to MHC class I, class II, non-classical, and MHC-related molecules, including ligands shown experimentally not to bind to any of these molecules.

5) Aid in the design of vaccines that include both antibody and T cell epitopes without the potential safety issues encountered using large proteins derived from dangerous pathogens or toxins.

6) Assist empirical studies by providing researchers with ready access to successful immunization approaches and outcomes, information on the size and structure of immunogens, and methods of generating and testing antibodies.

There is a strong need for the Immune Epitope Database and Analysis Resource described in this contract solicitation. The development and maintenance of a robust database and analysis resource will require a highly collaborative team composed of experts in database design and administration, computer programming, software engineering, bioinformatics, immunology, microbiology, biochemistry, computational biology, and website design and administration.

Statement of Work
Immune Epitope Database and Analysis Program
RFP DAIT-03-31

Independently, and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, materials, equipment, and facilities, not otherwise provided by the Government under the terms of this contract, as needed to perform the work set forth below. In addition, all licensing agreements entered into by the Contractor for completion of any or all of the tasks listed in the Statement of Work shall be transferable to the Government upon completion or termination of the contract. Specifically, the Contractor shall perform the tasks described in Parts A through E below**.**

A. **Establish and maintain a web-based relational database populated with antibody epitope and T cell epitope information**. The Contractor shall give particular attention to the inclusion of antibody and T cell epitopes associated with NIAID category A-C bioterrorism agents and their toxins, but shall also include epitopes derived from other emerging/re-emerging infectious pathogens, allergens, alloantigens, autoantigens, and model antigens, with the exception of HIV. Specifically, the database shall contain an organized compilation of amino acid or other molecular sequences of linear and conformational antibody epitopes, and an organized compilation of T cell epitopes consisting of peptide amino acid and other ligand sequences known to bind to various MHC class I, class II, non-classical, and MHC-related molecules of human, non-human primate, and other animal origin, including a sufficient number of HLA alleles to cover the human population worldwide. The database shall include the most current information available concerning each of the identified antibody and T cell epitopes, such as its three-dimensional structure, immunogenicity, neutralization capacity, other biological activities, source (pathogen or disease), and methods of epitope discovery and validation. All of the information contained within the Immune Epitope Database and Analysis Resource, as well as all of the contractor-generated materials (e.g., documentation, software source codes, analysis tools and algorithms), shall be made freely available to the research community for improvement and for publication purposes.

Specifically, the Contractor shall:

1) Within three (3) months of contract award, submit a proposed implementation plan for the Immune Epitope Database and Analysis Resource, which must receive the approval of the Project Officer before it is implemented. In addition, NIAID Information Technology Specialists will review the plan for appropriate computer security measures and compatibility with existing NIAID computer and web systems. Details of the implementation plan are located at the end of the Statement of Work, task E.

[See Notes to the Offeror: 1, 2, 3, 4 and 5]

2) Populate the prototype database with sample data and supporting information obtained from other databases and studies reported in the literature. The data and supporting information shall include, but not be limited to the following:
    1. Antibody epitopes and mimetopes (structural or functional antigen mimics) including linear and conformational sites, identifiable by their epitope sequence (i.e., amino acid, carbohydrate, or lipid composition for linear and conformational antibody epitopes) as well as other key information currently available, such as their antibody isotype; pathogen, antigen or disease source; composition of natural, artificial, and modified amino acids (as may occur during post-translational modifications of whole molecules or ligands); and haptens associated with the epitope/mimetope.
    2. T cell epitopes and mimetopes consisting of peptide and non-peptide ligands identifiable by their epitope sequence (i.e., amino acid, carbohydrate, or lipid composition) including the composition of natural, artificial, and modified amino acids as may occur during post-translational modifications of peptide ligands, as well as other key information currently available, such as their MHC binding motif; MHC molecule; pathogen, antigen or disease source; and haptens associated with the epitope/mimetope.
    3. For both antibody and T cell epitopes, nucleotide and amino acid sequences shall be aligned according to standard practices and procedures as exemplified in major scientific journals (e.g., *Journal of Immunology* general information: http://www.jimmunol.org/misc/ifora.shtml , specifications for styles: http://www.jimmunol.org/misc/authorstyle.shtml) and/or existing databases (e.g,.Genbank, SwissProt, and/or MHC-ligand databases previously listed under Background Information).

4. Extensive annotation for each antibody and T cell epitope, which shall include:
    i. Size and three-dimensional structure of the antigen from which the epitope derives, as well as the MHC-ligand or antigen-antibody complexes, where available.
    ii. Epitope location on the whole antigen (where available).
    iii. Background information about the epitope, including: identification methods; validation of immunogenicity and/or antigenicity *in vivo* and *in vitro* (e.g, protection studies *in vivo*, *in vitro* cytotoxicity, ELISA, ELISpot, pathogen neutralization); methods to generate and test antibodies; antibody/antigen binding affinity and immunogenicity; post-translational modifications; and MHC binding affinity.
    iv. Full references (i.e., the PubMed identification number, source, and link to the PubMed website).

[See Notes to the Offeror: 6]

3) Annotate the prototype database using widely accepted and appropriate biological ontologies, as can be found in Medical Subject Headings (MeSH) and Unified Medical Language (UMLS) concepts, where applicable, or the Contractor-developed ontologies (see Section E.9 of the Statement of Work). Ensure that domain experts in immunology perform the data annotation. Minimally, the domain experts shall comprise a group of scientists with expertise in the fields of antigen processing and presentation for generation of T cell epitopes, antibody production, antibody-antigen binding, and B and T cell activation. Domain experts in immunology and other related fields (e.g., biochemistry, microbiology, computational biology, genetics) shall work closely with database development and software engineering staff to ensure that the scientific information is catalogued and organized in a manner that permits users to access specific data through intelligent data searches and queries. For example, domain experts may develop a list of possible queries and test these queries to determine whether accurate and comprehensive information is retrieved from the database. Then contract staff shall make appropriate adjustments to the database and software systems to improve user access to information within the database.

4) Beta-test the prototype database system and modify it accordingly to ensure that the features and contents of the database meet the required specifications. The Contractor shall:
    a) Establish a private website for beta-testing which will later be converted to a publicly accessible, central website for the Immune Epitope Database and Analysis Resource.
    b) Ensure that each of the following features of the prototype database system is thoroughly beta-tested by the Contractor:
        i. The central website and FTP website (both of which will be private websites during beta-testing) and their help features.
        ii. The three methods for populating the database with epitope data and supporting information: data transfer from other databases; direct web-based data submissions; and data entry from studies reported in the literature.
        iii. Annotation and curation practices the Contractor will use for the information in the database.
        iv. Procedures that the Contractor will use to maintain the database, central website, and FTP website, including methods for system backup and recovery.
        v. Methods the Contractor will use to produce monthly status reports.
        vi. Tools for the user to locate information in the database, such as browsing, querying, and data mining tools.
        vii. Tools for the user to analyze information in the database, such as standard data analysis tools, algorithms, and mathematical models.
        viii. Help features provided at the Database and Analysis Resource website, including access to FAQs, online (email) and/or telephone assistance, and user bulletin board.
        ix. Capability for multiple users to concurrently access the central website, FTP website, web-based data entry, and their help features, conduct queries, retrieve information, and use the other analytical tools.
    c) Provide training for domain experts in the fields of immunology, microbiology, and bioinformatics, including members of the Scientific Advisory Committee (SAC), on how to access and use the various features of the prototype database system.
    d) Ensure that each of the following features of the prototype database system is thoroughly beta-tested by the domain experts and SAC members:
        i. The central website and FTP site and their help features.

ii. Tools for the user to locate information in the database, such as browsing, querying, and data mining tools.
iii. Tools for the user to analyze information in the database, such as standard data analysis tools, algorithms, and mathematical models.
iv. Capability for multiple users to concurrently access the central website, FTP website, and their help features; data submission and annotation functions; conduct queries; retrieve information; and use the other analytical tools.

5) Provide a final implementation plan for the Immune Epitope Database and Analysis Resource within 18 months of contract award, which includes all of the features specified in Section A.1 - 3 and E of the Statement of Work, addresses the problems encountered during beta-testing, and incorporates the recommendations of the Project Officer, NIAID Information Technology staff, and Scientific Advisory Committee.

6) Following Project Officer and SAC approval, populate the Immune Epitope Database with all available antibody and T cell epitopes and supporting information, as specified in Section A.2 of the Statement of Work. The data shall be obtained from established databases, direct web-based submissions by individual research laboratories and biotechnology companies, and studies reported in the literature. In order to facilitate submission of proprietary data to the database, the Contractor shall develop, in conjunction with the Project Officer, a Transfer Agreement (TA) for investigator-initiated direct web-based submissions. Each individual research laboratory, prior to submission of their proprietary data to the database, shall complete the TA. Transfer agreements are not required for transfer of data from existing databases or studies reported in the literature, unless requested by the data source. Contractor will be responsible for maintaining an up-to-date filing system for maintaining these agreements for transfer of data and for ensuring that data is transferred under an appropriate agreement.

7) Establish and maintain a publicly accessible, central website and FTP website for the Immune Epitope Database and Analysis Resource that include the features specified in Section E.14 and E.15 of the Statement of Work.

8) Maintain the Immune Epitope Database and Analysis Resource, as specified in Section E.16 of the Statement of Work.

[See Notes to the Offeror: 4]

B. **Establish and maintain an Analysis Resource for the Immune Epitope Database,** in consultation with and final approval by the Project Officer before finalizing tasks 1 – 3 below. Specifically, the Contractor shall:

1) Provide online access, through links on the central website, to standard analytical tools to help researchers locate and analyze information contained in the database, including, but not limited to:
   a) Software tools for data mining and analysis of antibody and T cell epitope information.
   b) Algorithms, mathematical models, and other prediction tools for identifying novel antibody and T cell epitopes from genome and protein sequence information. The Contractor shall provide information to the user community on the reliability and accuracy of these tools, including their strengths and weaknesses.

2) Provide online access to other relevant databases and related information. These links shall be checked monthly by the Contractor for accessibility to intended web site. The links shall include, but not be limited to:
   a) Genome sequence databases for mammalian and non-mammalian organisms (including prokaryotes).
   b) Protein databases.
   c) Other MHC-peptide databases, such as the HIV Molecular Immunology Database, that contain information not found in the Immune Epitope Database and Analysis Resource.

3) Develop improved analytical tools, wherever possible, that will be accessible to the scientific community via the central website, including, but not limited to:
   a) Improved software tools for data mining and analysis of antibody and T cell epitope information.
   b) New predictive algorithms capable of accumulating information and improving as data increases, for identifying potential epitopes from a gene, protein, or pathogen of interest. These algorithms may integrate proteolytic cleavage site identification and prediction of potential post-translational modifications.

c) Advanced algorithms and mathematical models for predicting host immune responses to particular antibody and T cell epitopes. All novel analytical software tools shall be tested and validated by the domain experts and SAC members prior to release on the central website. New technologies shall be incorporated when available to improve the knowledge base and help researchers use the more advanced analytical tools.

4) Provide a quarterly newsletter for the scientific community and an annual compendium of data in the Immune Epitope Database and all analysis tools developed during the previous year. The newsletter and compendium shall be on-line publications available at the central website. The newsletter shall be available at the website on the 15th of the month following the end of each quarterly performance period; and, the annual compendium shall be available at the website on the 30th of the month following yearly anniversary of the contract. A hard copy of the newsletter and the compendium shall be sent to the Project Officer two weeks prior to posting at the website.
   a) The quarterly newsletter shall include, but not be limited to:
      i. An overview and update of the antibody and T cell epitope information in the Immune Epitope Database, highlighting new epitopes added since publication of the previous newsletter.
      ii. An overview and update of the key features of the website, highlighting new analytical tools available through the Analysis Resource and other improvements since publication of the previous newsletter.
      iii. A summary of major scientific publications and breakthroughs for which the Immune Epitope Database and Analytical Resource played a contributory role or had a direct impact on the database that occurred since publication of the previous newsletter (e.g., development of novel or improved analytical tools for epitope detection, identification, or prediction; identification of a highly significant antibody or T cell epitope).
   b) The annual compendium shall include, but not be limited to:
      i. A comprehensive list and description of the antibody and T cell epitope information in the Immune Epitope Database, identifying new epitopes added since publication of the previous compendium.
      ii. A comprehensive list and description of the various features of the website, particularly the analytical tools available through the Analysis Resource, identifying new features added since publication of the previous compendium.
      iii. A comprehensive list and description of major scientific publications and breakthroughs for which the Immune Epitope Database and Analytical Resource played a contributory role or had a direct impact on the database that occurred since publication of the previous compendium.

5) Provide ad hoc reports to the Project Officer on subsets of data within the Immune Epitope Database that fall within NIAID's mission, including, but not limited to, data relevant to biodefense, emerging/re-emerging infectious diseases, autoimmunity, asthma, allergy, and transplantation. These reports may not be for public use, but the information contained within the reports may be provided to various branches of the Government and/or other public health – related agencies upon request. The Project Officer will specify the report format at the time of request.

C. **Maintain close ties to the scientific community.** Specifically, the Contractor shall:

1) In conjunction with the Project Officer, establish a Scientific Advisory Committee (SAC) composed of experts in the fields of immunology, microbiology, biochemistry, bioinformatics, software engineering, database development, and computational biology who represent a broad range of areas, including but not limited to: antigen processing and presentation, antibody and T cell epitope discovery, high throughput methods for epitope identification, antibody production, B and T cell activation, bioinformatics, software design and implementation, computational biology, and database and website development. The SAC shall provide advice to the Contractor and to the NIAID on the needs of the scientific community regarding the development and use of the Immune Epitope Database and the accompanying data analysis tools and predictive algorithms in the Analysis Resource. The Contractor shall be responsible for:
   a) Recommending selection criteria for SAC members, including a proposed distribution of membership by area of expertise and other relevant selection factors. The Contractor shall not contact specific individuals regarding service on the SAC.
   b) Recommending a timeline for SAC meetings or conference calls convened to solicit advice and recommendations from SAC members.
   c) Organizing SAC meetings and conference calls, and providing summary reports of the meetings, including SAC recommendations, to the Project Officer.

2) Interact with the scientific community by:
    a) Promoting awareness throughout the scientific community of the data and tools available through the Immune Epitope Database and Analysis Resource. At a minimum, information should be disseminated via electronic and print media and presentations at scientific meetings, symposia, and workshops.
    b) Sponsoring an annual workshop to improve the contents of the database, standardize methodologies (e.g., antibody and T cell epitope identification, binding assays, validation of epitope antigenicity *in vitro* and *in vivo*), develop improved data mining and analysis tools and more robust algorithms, and promote technology transfer. In consultation with the Project Officer, the Contractor shall annually identify key contributors to the fields of immunology, microbiology, biochemistry, computational biology, and bioinformatics whose contributions are relevant to the Immune Epitope Database and Analysis Resource, and invite them to participate in the next workshop. Within eight (8) weeks of the completion of the workshop, the Contractor shall provide the Project Officer with a hard copy and electronic version of a detailed summary of the workshop, including an executive summary highlighting participants' contributions and the recommendations that emerged from the meeting. After Project Officer approval, the Contractor shall post the executive summary on the central website.
    c) Interacting with investigators on an ongoing basis to solicit feedback from users and address questions that arise. These interactions shall include web-based discussions (offered through the central website) and participation at scientific meetings, symposia, and workshops.

[See Notes to the Offeror: 7]

D. **Submit a proposed transition plan** detailing how the complete Immune Epitope Database and Analysis Resource including all accompanying source codes (for access to the database structure), DTDs, programming software, ontology and logical methods (SOPs) for applying the ontology to the database, accumulated data, all analytical tools developed by the Contractor or incorporated into the Analysis Resource from other sources, and equipment will be transferred in an orderly manner to the Government or a subsequent contractor upon completion of the contract. The proposed transition plan shall be due twelve (12) months before the contract's expiration date. The plan shall include but not be limited to: a comprehensive inventory of all the data, websites, software tools, analytical tools, ontology, and technology developed, accumulated, and distributed during the contract's performance as well as a list containing detailed descriptions of all process documentation (e.g., hard copy and electronic versions of all standard operating procedures) developed during the contract's performance. The plan shall also include recommended disposition of hardware and software necessary to sustain activities provided for in the contract. The Contractor shall work with the Project Officer, Contracting Officer, and NIAID Information Technology Specialists to refine and complete this plan. The final transition plan shall be delivered no later than six (6) months before the contract's expiration date.

E. **Submit, within 3 months of award, a proposed implementation plan** for the Immune Epitope Database and Analysis Resource (as listed under task A) that shall include, but not be limited to:

1. A description of and rationale for using the Contractor-recommended database management system, which shall be a commercially available and supported relational database management system that incorporates Structured Query Language (SQL) and allows users to search the database using query by example (QBE).
2. The proposed logical structure of the database system, which shall include the following features:
    a) Software strategy that makes the data portable and usable across platforms, including documentation and validation of best practices in software engineering processes.
    b) Capability to view information (conduct queries) based on any type of epitope, antigen, and/or pathogen-specific information maintained in the database and retrieve all of the information relevant to that particular epitope. For example, each epitope may be assigned a unique epitope identifier for use in linking the different types of epitope-specific information. In addition, the Contractor shall provide detailed descriptions of the processes for viewing the information contained within the database.
    c) Use of XML or another explicitly defined parsable format.
    d) The process for data representation (e.g. Document Type Definitions (DTD)) and the rationale for choosing this representation that is based upon the desired functionality of the system.
    e) Internet accessibility.
    f) Capacity to actively maintain at least a million entries each for T cell and antibody epitope information and accompanying data (see paragraph A.2 for details), with a plan to expand capacity by at least ten-fold (1000%) within two years.
    g) Flexibility, adaptability, and responsiveness to the changing needs of the scientific community.

3. The types of standard application programs that will be available to users accessing the database via the Internet.

4. The types of security systems, firewalls, and computer virus detection systems that will be used to ensure database and website protection.
5. Detailed information on the computer facilities, hardware, and software that will be used by the Contractor to design, develop, populate, and maintain the database (including data storage capacity and the database design and querying tools to be used by the Contractor).
6. Software applications for populating and updating the database with epitope data and supporting information obtained from other databases, direct website submissions, and studies reported in the scientific literature. Procedures for direct website submissions shall enable individual research laboratories and biotechnology companies to submit antibody and T cell epitope data and supporting information directly to the database. The implementation plan shall include how the Contractor proposes to incorporate epitope-related data resulting from systematic studies of MHC-ligand binding, including ligands that have been proven to be unable to bind particular MHC molecules or antibodies. This information shall be obtained from other databases, direct website submissions, and studies reported in the scientific literature. The Contractor shall be responsible for updating the database at least once a month to incorporate the most recent information obtained from other databases, direct website submissions, and studies reported in the literature.
7. Standard operating procedures for developing and maintaining quality control and uniform standards for data entry and the transfer of data from other databases, direct website submissions, and studies reported in the literature; procedures for developing and maintaining uniform standards for epitope representation; procedures to ensure that all of the information maintained in the database and posted on the central website is internally consistent; and procedures to help the user community identify newly added information and navigate between epitope data, supporting information, and links to other web-based databases and relevant information.
8. Strategy for adapting existing, building, and/or maintaining a robust ontology that accurately represents the information contained within the database and analysis resource. Domain experts in immunology and other qualified members of the Contractor's staff shall adapt or develop the ontology, with input from the SAC and final approval by the Project Officer.
9. Methods and approaches for applying the contractor developed ontology, which may incorporate existing ontologies, to data annotation and management (curation) procedures for the information in the database. These methods shall also include, but not be limited to, how the Contractor proposes to ensure that the information in the database is valid and up-to-date; that data archiving permits linkages between original submission data and subsequent updates from the same or different sources, including correspondence with investigators; and that the data will be accurately preserved over time, assuming future changes in technology.
10. Methods for viewing (browsing and querying) the information in the database, including how the Contractor proposes to define and use a controlled vocabulary (e.g., keywords and synonyms) and text strings in intelligent data searches. At a minimum, there shall be the capability for users to view by antibody epitope sequence, T cell epitope sequence, antibody isotype, MHC binding motif, MHC molecule, antigen, DNA sequence, source organism, disease, peptide or ligand structural modifications (e.g. glycosylated, haptenated, sulfonated, nitrated), and literature reference (author, journal, publication date, keywords, PubMed identification number).
11. Capability for users to customize search result reports.
12. Methods for analyzing information in the database, including how the Contractor proposes to identify and test standard software tools for data mining and analysis, predictive algorithms, mathematical models, and other analytical tools.
13. Methods for developing improved algorithms, models, and other more sophisticated analytical tools for use in discovering new knowledge from the database.
14. Procedures for securing, developing, and maintaining efficient and unencumbered Internet access to the Immune Epitope Database and Analysis Resource. The plan shall include the establishment of a central website as well as a separate File Transfer Protocol (FTP) website to expedite the downloading of data to user workstations. Both websites must allow concurrent access by multiple users.
15. Methods for providing technical assistance to help users access the database and use the accompanying data analysis tools. At a minimum, the central website for the database shall provide answers to Frequently Asked Questions (FAQs), offer other types of technical assistance (e.g., responses to user questions via email and/or telephone), and offer web-based discussion boards for the scientific community. The Contractor shall respond to individual user inquiries and problems within 24 hours (including weekends and holidays).
16. Procedures for maintaining the database and websites, including routine system backup and recovery. The Contractor shall be responsible for creating daily backup files of the entire Immune Epitope Database and Analysis Resource. It is anticipated that the server shall be housed at the Contractor's work site. An additional backup server shall be housed at the NIAID. This server shall have identical information to the server at the Contractor's work site and shall be backed-up daily. The Contractor shall work with NIAID Information Technology staff to ensure that both servers contain identical information and comply with NIAID computer security practices and procedures. In addition to describing backup and recovery procedures, the plan shall include how the Contractor proposes to maintain the integrity of the database software, including the installation of hardware and software upgrades on both

servers while maintaining accessibility to the user community. NIAID Information Technology staff will periodically review the system specifications and make recommendations for system upgrades, which will be communicated to the Contractor through the Project Officer.

17. Methods for obtaining and summarizing the information to be submitted to the Project Officer in monthly status reports, which shall include:
    a) Total number of external visits to the central website and FTP website (number of hits), as well as more detailed descriptions of website usage.
    b) Number of requests for technical assistance and the types of assistance provided, including average Contractor response times and user feedback.
    c) New information added to the database.
    d) New tools developed and/or integrated into the Database and Analysis Resource.
    e) Total number of database entries by different types.
    f) Links to other websites, and verification of web site accessibility by the links thorough monthly quality control procedures (e.g., link-checking programs).
    g) Any changes in the structure or management of the database system, central website, and/or FTP website.
18. Methods for complying with Section 508 of the Americans with Disabilities Act (ADA).
19. A plan and proposed timeline (with specific milestones and other performance measures) for developing and beta-testing a prototype Immune Epitope Database populated with sample data and a prototype Analysis Resource that includes different types of data analysis tools, algorithms, and mathematical models.

Notes To Offerors

Immune Epitope Database and Analysis Program
DAIT-03-31

NOTE 1

For the purpose of this contract solicitation, the term "T cell epitope" will include all ligands (derived from proteins, carbohydrates or lipids) bound to any member of the family of MHC and MHC-related molecules, thus encompassing all MHC-ligand complexes that are known to or have the potential of triggering T cell responses.

NOTE 2

Subcontracting agreements are acceptable and are encouraged in order to accomplish the work outlined in this solicitation. The proposal must describe in detail a management plan defining how the Contractor will coordinate the work of the Subcontractor(s). The proposal must also define the Subcontractors' contributions to the overall proposal, and include a complete description of all Subcontractors' duties, facilities, professional background of personnel, and costs.

NOTE 3

Disclosures of any and all patents and copyrights or patent and copyright applications of database design, analysis tools, or procedures filed in or outside the US by the Offerors and/or listed personnel or collaborators must be made at the time of proposal submission and updated in quarterly progress reports. Individual and institutional intellectual property rights and rights to inventorship under United States patent law will not be affected by participation in this RFP. The involvement of the NIH in the performance of this contract will not affect ownership rights of the participating parties beyond U.S. Government rights under any funding agreement as specific under 35 U.S.C. #202.

It is expected that the Offeror will administer their patent rights in a manner that will not conflict with the central goal of this RFP, which is to make the database and analysis resource freely available to the research community.

All licensing agreements entered into by the Contractor for completion of any or all of the tasks listed in the Statement of Work shall be transferable to the Government.

NOTE 4

The following guidelines are provided for the Technical Proposal preparation:

The Technical Proposal shall include documentation of the qualifications, knowledge, experience, education, competence, and decision-making skills of the proposed key personnel. In addition, similar documentation shall be provided for technical and administrative staff proposed to carry out the requirements of this contract. Documentation shall include all previous and current projects of a similar nature, including the grant or contract number, the sponsoring agency, the Project Officer, and description of the project. The Offeror shall include Curricula Vitae of all proposed personnel in the proposal. In addition, the Offeror shall describe the responsibilities and levels of effort of all proposed personnel who are assigned to the contract, including subcontractors. The Offeror shall provide all costs associated with the proposed personnel in the Business Proposal. The cost information required in the Technical Proposal is a summary of the hours proposed for each individual and direct costs for each cost category by contract year. Total **Direct** Costs by contract year must also be furnished in the Technical Proposal.

The Offeror shall include key personnel with strong expertise in scientific areas critical to development, operation and maintenance of the database (e.g., database and web design experts, software engineers, bioinformatics specialists, immunologists, microbiologists, biochemists, computational biologists, mathematicians, computer scientists).

The Offeror shall provide a detailed description of the methods and procedures for accomplishing tasks A-E, outlined in the Statement of Work, that shall minimally include a plan and proposed timeline (with specific milestones and other performance measures) for developing and beta-testing a prototype Immune Epitope Database populated with sample data and a prototype Analysis Resource that includes different types of data analysis tools, algorithms, and mathematical models.

The Offeror shall provide logical and physical database models.

The Offeror shall discuss the merits of using XML or other mark-up language regarding the strengths and limitations that it provides to the overall system.

All data and other information needed to evaluate the Offeror's proposed systems (e.g., models, flow charts, graphics, tables, and figures) shall be included as part of the proposal.

The Offeror may submit a static or animated model as a hard copy or CD-rom, respectively, of the proposed database interface.

The Offeror may submit a prototype for inclusion of 3-dimensional structures as a static (hard copy) or animated model (CD-rom) for antigenic epitopes, whole antigens, and/or antibody-antigen interactions and relevant information, where available.

The Offeror shall not include live links to websites within the proposal to describe or demonstrate the database interface or any other prototypes or models for the Immune Epitope Database and Analysis Resource.

Experts in related fields shall perform the data annotation and curation and the Offeror shall provide justification for staffing data annotation and curation positions. These experts shall also work closely with software engineering in development of query, data analysis, and data mining software tools and algorithms.

The Offeror shall provide a plan for upgrading the database that includes specific criteria for upgrades, estimated down-time during upgrade, estimated number of upgrades required for life of contract, projected effect on compatibility with users' systems, and strategy to minimize interruption of community accessibility to the database.

NOTE 5

The Offeror shall provide specific descriptions of available equipment and facilities to conduct the work outlined in this contract. In addition, the Offeror shall provide a plan for maintaining the computer server (one backup server shall be housed at the NIAID Extramural Information Technology Branch), creating data back-up files (shall occur nightly), providing security systems for the database, and computer virus detection and elimination methods.

NOTE 6

All providers of data for inclusion in the database and/or analysis resource and investigators who have contributed directly to the data generation will be cited, either by authorship or acknowledgement of their contributions. These citations will be visible to the scientific community that uses the database and analysis resource.

NOTE 7

For budget estimating purposes, assume the following:

The annual Scientific Advisory Committee meeting cost estimates should include travel costs (transportation, meals, hotel, etc.) for the Committee members and appropriate Contractor staff, as well as costs associated with holding the meeting. All cost estimates should be based on Government rates for per diem, hotel and transportation (coach class). Assume the meetings will be held in Bethesda, MD, for 1 day.

The annual workshop cost estimates should include travel costs (transportation, meals, hotel, etc.) for 20 invited participants, as well as costs associated with holding the workshop. All cost estimates should be based on Government rates for per diem, hotel, and transportation (coach class). Assume the workshop will be held in Bethesda, MD, for 1.5 days.

The Offeror shall budget travel for key personnel to attend two scientific meetings per year. All cost estimates should be based on Government rates for per diem, hotel and transportation (coach class).

The Offeror shall budget for developing and publishing (web-based, on-line) a quarterly newsletter and an annual compendium for the Immune Epitope Database and Analysis Resource. The Offeror also shall budget for the generation of two-three (2-3) ad hoc reports per year as requested by the Project Officer.

The Offeror shall budget for informing the scientific community of the existence of the Database and Analysis Resource and for promoting use of this database by the community. Notification shall be done by advertising in scientific journals such as Science, Nature, Immunity, Journal of Experimental Medicine, Infection and Immunity, Virology, Journal of Virology; at

scientific meetings, workshops and symposia; and through Professional Societies such as the American Association of Immunologists (AAI) and the American Society of Microbiologists (ASM).

The Government estimates that the performance of the activities presented in the Statement of Work will require a dedicated database server, a dedicated web serve, substantial personnel including the Principal Investigator, System Analyst (Project Lead), Senior Scientist/Immunology Group lead (data annotation and curation), Database Designer, Web Designer, Program Analysts (programmers), Scientists (data annotation and curation), Quality Assurance/Testers, Database Administrator, and Web Administrator. These estimates are for the Contractors' information only and are not to be considered restrictive for proposal purposes. The Government's estimate of the level of effort required for this RFP is included for guidance only in SECTION L – INSTRUCTIONS, CONDITIONS AND NOTICES TO OFFERORS – Paragraph e. ESTIMATE OF EFFORT. This estimate, also, in Section L is not considered restrictive for proposal purposes.

NOTE 8

Offerors shall submit a cost proposal for a full 7-year period, which will include the 5 year contract period and 2 one-year option periods. The two option years may or may not be exercised.

Reporting Requirements
Immune Epitope Database and Analysis Program
RFP DAIT-03-31

REPORTING REQUIREMENTS AND DELIVERABLES

As part of the work to be performed under this contract, the Contractor shall prepare and deliver the following reports throughout the period of work. The exact submission schedule will be negotiated and established in the contract document.

I. Immune Epitope Database and Analysis Resource Hardware and Software Implementation Plan

The Contractor shall submit two (2) copies on the final day of the third month following the award of the Contract. The original shall be submitted to the Project Officer, with a copy to the Contracting Officer. Each Implementation Plan shall include the following:

(A) Face page to include contract number, contract title, performance period covered, contractor's name and address, telephone and telefax numbers, E-mail address, and report submission date.

(B) A full description as described in the Statement of Work (paragraph A.1.).

II. Quarterly Progress Reports

The Contractor shall submit two (2) copies on the 15th of the month following the end of each quarterly performance period. The original shall be submitted to the Project Officer, with a copy to the Contracting Officer. Each Quarterly report shall include the following:

(A) Face page to include contract number, contract title, performance period covered, contractor's name and address, telephone and telefax numbers, E-mail address, and report submission date.

(B) An executive summary, to include, but not be limited to:

1) An overview of the status of the Database and Analysis Resource including personnel, database development activities, software analysis and development, new entries to the database (peptide, non-peptide ligand, and antibody epitope and accompanying data);
2) A brief overview of the work completed during the current reporting period and/or justification for failure to complete intended work or performance of unintended work; and
3) A brief overview of activities that occurred during the current reporting period and any problems (technical or financial) that occurred during the current reporting period.

(C) A full description of:

1) The work performed during the reporting period including progress on database, analysis resource and accompanying software design and development such as database structure, query tools, software development for tracking and retrieving data in the database, predictive algorithms, data analysis and mining tools, and an update on tracking community feedback and use of the database including improvements to the database or website based community comments;
2) The relation between the accomplishments and the goals and objectives of the contract; and
3) Explanations of any differences between planned and actual progress, and, if necessary, what corrective steps are planned or have been implemented.

(D) Copies of manuscripts (published or unpublished) derived from research performed under the contract and copies of all abstracts, manuscripts, preprints, and publications that resulted from work conducted or any protocol or method developed specifically under this contract during the performance period.

(E) A full disclosure of intent to file patent applications or copyrights within or outside of the U.S. on database design, software tools (e.g. algorithms, data analysis, and data mining tools), or other procedures derived or established by the work supported under this contract; full disclosure of patent applications or copyrights filed, as well as copies of patent or copyright applications.

Quarterly Progress Reports are not required for periods in which an Annual or Final Report is due.

III. Annual Progress Reports

The Contract shall submit two (2) copies (as specified above) of Annual Progress Reports that document and summarize the results of the entire contract work for the period covered. This report shall be due the 30th of the month following each yearly anniversary date of the contract. An Annual report shall not be due when the Final Report is submitted. The report shall conform to the following format:

(A) Face page to include contract number, contract title, performance period covered, contractor's name and address, telephone and telefax numbers, E-mail address, and report submission date.

(B) An executive summary to include program progress, problems encountered, resolutions for all problems encountered, and plans for the upcoming year;

(C) Detailed description of the work performed and how it fulfills the goals set in the implementation plan (year 1) or plans defined in the previous annual report (years 2 – 4); relation to work being conducted in the area by other groups; problems encountered during the year; plans or methods to resolve the problems; current impact on the scientific community based on annual meeting reports, community survey, and tracking of database usage by the community; and plans for the upcoming year.

IV. Final Report

The Contractor shall submit two (2) copies (as specified above) of the Final Report that document and summarize the results of the entire contract period of performance. This report shall be submitted on or before the completion date of the contract. The report shall conform to the following format:

(A) Face page to include contract number, contract title, performance period covered, contractor's name and address, telephone and telefax numbers, E-mail address, and report submission date.
(B) Introduction covering the purpose and scope of the contract effort including a summary of salient results. The Contractor shall submit a summary, not to exceed 200 words, of salient progress achieved during performance of the contract;
(C) An executive summary, to include fulfillment of goals and of the specific aims set forth in the proposal; and

(D) A detailed description of the work performed during the contract period including, but not limited to, database design, development and population; a description of the types of information contained within the database, such as number and type of epitopes); a detailed description of analysis tools available through the Analysis Resource; how the developed Database and Analysis Resource fulfilled the goals of the original contract proposal and implementation plan; problems encountered during the contract period; measures used to resolve the problems; and current impact of the Immune Epitope Database and Analysis Resource on the scientific community based on annual meeting reports, community survey, and tracking of database usage by the community.

Deliverable Reports	No. of Copies	Addressee/Distribution	Due Dates
Database and Analysis Resource Software Implementation Plan	2	Project Officer NIAID Room 5138 6700-B Rockledge Drive Bethesda, MD 20892-7640 FedEx Zip Code 20817	On or before the 30th of the third month following Contract Award
Quarterly Newsletter and Annual Compendium	2	Project Officer NIAID Room 5138 6700-B Rockledge Drive Bethesda, MD 20817-7640 FedEx Zip Code 20817	Two weeks prior to posting the documents on the database and Analysis Program Website: Newsletter shall be available at the website on the 15th of the month following the end of each quarterly performance period; the annual compendium shall be available at the website on the 30th of the month following yearly anniversary of the contract. available
Quarterly Reports	2	Project Officer NIAID Room 5138 6700-B Rockledge Drive Bethesda, MD 20892-7640 FedEx Zip Code 20817	The 15th of the month following the end of each quarterly performance period
Annual Reports	2	Project Officer NIAID Room 5138 6700-B Rockledge Drive Bethesda, MD 20892-7640 FedEx Zip Code 20817	The 30th of the month following yearly anniversary of the contract
Draft and Final Transition Plan	2	Project Officer NIAID Room 5138 6700-B Rockledge Drive Bethesda, MD 20892-7640 FedEx Zip Code 20817	Draft – 12 months prior to the contract end date Final- 6 months prior to contract end date
Final Report	2	Project Officer NIAID Room 5138 6700-B Rockledge Drive Bethesda, MD 20892-7640 FedEx Zip Code 20817	On or before the completion date of the contract

I. Other Deliverables

The Contractor shall return to NIH or deliver to a successor Contractor (as directed by the Project Officer) on or before the contract completion date:

A. All equipment supplied or procured under this contract, including the computer server;

B. The complete Immune Epitope Database and Analysis Resource including, but not limited to, all of the information contained within the database and analysis resource; licenses obtained for use of commercially available databases, software, and other materials used in the design, development, population and maintenance of the Database and Analysis Resource; accompanying source codes for the database; DTDs; and programming software;

C. Ontologies developed for annotation and curation of the database; and

D. All data analysis software tools including predictive algorithms and data analysis and mining tools developed or made available to the research community through the website during the contract period, including all licenses acquired for inclusion of commercially or privately- developed algorithms and tools to the Analysis Resource.

PART I - THE SCHEDULE

SECTIONS B - H -- UNIFORM CONTRACT FORMAT - GENERAL

1. **A Sample Uniform Contract Format may be found at the following website:**

   http://www4.od.nih.gov/ocm/contracts/rfps/sampkt.htm

2. **Disregard SECTION I and J of this sample. Those SECTIONS have been incorporated as part of this RFP.**

PART II – CONTRACT CLAUSES

SECTION I - CONTRACT CLAUSES

3. **THE FOLLOWING PAGES CONTAIN A LISTING(S) OF GENERAL CLAUSES WHICH WILL BE APPLICABLE TO MOST CONTRACTS RESULTING FROM THIS RFP. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR(S) WILL DETERMINE THE SPECIFIC GENERAL CLAUSES LISTING TO BE CONTAINED IN THE CONTRACT(S) AWARDED FROM THIS RFP.**

ARTICLE I.1. GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT – FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

This contract incorporates the following clauses by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. Also, the full text of a clause may be accessed electronically at this URL: http://www.arnet.gov/far/.

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CHAPTER 1) CLAUSES

FAR Clause No.	Date	Title
52.202-1	Dec 2001	Definitions
52.203-3	Apr 1984	Gratuities (Over $100,000)
52.203-5	Apr 1984	Covenant Against Contingent Fees (Over $100,000)
52.203-6	Jul 1995	Covenant Against Contingent Fees (Over $100,000)
52.203-7	Jul 1995	Anti-Kickback Procedures (Over $100,000)
52.203-8	Jan 1997	Cancellation, Rescission, and Recovery of Funds for Illegal or Improper Activity (Over $100,000)
52.203-10	Jan 1997	Price or Fee Adjustment for Illegal or Improper Activity (Over $100,000)
52.203-12	Jun 1997	Limitation on Payments to Influence Certain Federal Transactions (Over $100,000)
52.204-4	Aug 2000	Printing/Copying Double-Sided on Recycled Paper (Over $100,000)
52.209-6	Jul 1995	Protecting the Governments Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment (Over $25,000)
52.215-2	Jun 1999	Audit and Records - Negotiation (Over $100,000)
52.215-8	Oct 1997	Order of Precedence – Uniform Contract Format
52.215-10	Oct 1997	Price Reduction for Defective Cost or Pricing Data
52.215-12	Oct 1997	Subcontractor Cost or Pricing Data (Over $500,000)
52.215-14	Oct 1997	Integrity of Unit Prices (Over $100,000)
52.215-15	Dec 1998	Pension Adjustments and Asset Reversions
52.215-18	Oct 1997	Reversion or Adjustment of Plans for Post-Retirement Benefits (PRB) Other Than Pensions
52.215-19	Oct 1997	Notification of Ownership Changes
52.215-21	Oct 1997	Requirements for Cost or Pricing Data or Information Other Than Cost or Pricing Data - Modifications
52.216-7	Feb 2002	Allowable Cost and Payment
52.216-8	Mar 1997	Fixed Fee
52.219-8	Oct 2000	Utilization of Small Business Concerns (Over $100,000)

52.219-9	Jan 2002	Small Business Subcontracting Plan (Over $500,000)
52.219-16	Jan 1999	Liquidated Damages - Subcontracting Plan (Over $500,000)
52.222-2	Jul 1990	Payment for Overtime Premium (Over $100,000) (NOTE: The dollar amount in paragraph (a) of this clause is $0 unless otherwise specified in the contract.)
52.222-3	Aug 1996	Convict Labor
52.222-26	Apr 2002	Equal Opportunity
52.222-35	Dec 2001	Equal Opportunity for Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans
52.222-36	Jun 1998	Affirmative Action for Workers with Disabilities
52.222-37	Dec 2001	Employment Reports on Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans
52.223-6	May 2001	Drug-Free Workplace
52.223-14	Oct 2000	Toxic Chemical Release Reporting
52.225-1	May 2002	Buy American Act - Supplies
52.225-13	Jul 2000	Restrictions on Certain Foreign Purchases
52.227-1	Jul 1995	Authorization and Consent, Alternate I (Apr 1984)
52.227-2	Aug 1996	Notice and Assistance Regarding Patent and Copyright Infringement (Over $100,000)
52.227-11	Jun 1997	Patent Rights - Retention by the Contractor (Short Form) (NOTE: In accordance with FAR 27.303 (a) (2), paragraph (f) is modified to include the requirements in FAR 27.303 (a) (2) (i) through (iv). The frequency of reporting in (i) is annual.
52.227-14	Jun 1987	Rights in Data – General
52-232-9	Apr 1984	Limitation on Withholding of Payments
52.232-17	Jun 1996	Interest (Over $100,000)
52.232-20	Apr 1984	Limitation of Cost
52.232-23	Jan 1986	Assignment of Claims
52.232-25	Feb 2002	Prompt Payment
52.232-34	May 1999	Payment by Electronic Funds Transfer--Other Than Central Contractor Registration
52.233-1	Dec 1998	Disputes
52.233-3	Aug 1996	Protest After Award
52.242-1	Apr 1984	Notice of Intent to Disallow Costs
52.242-3	May 2001	Penalties for Unallowable Costs (Over $500,000)
52.242-4	Jan 1997	Certification of Final Indirect Costs

52.242-13	Jul 1995	Bankruptcy (Over $100,000)
52.243-2	Aug 1987	Changes - Cost Reimbursement, Alternate V (Apr 1984)
52.244-2	Aug 1998	Subcontracts, Alternate II (Aug 1998) *If written consent to subcontract is required, the identified subcontracts are listed in ARTICLE B., Advance Understandings.
52.244-5	Dec 1996	Competition in Subcontracting (Over $100,000)
52.245-5	Jan 1986	Government Property (Cost-Reimbursement, Time and Material, or Labor Hour Contract)
52.246-24	Feb 1997	Limitation of Liability-High-Value Items
52.249-6	Sep 1996	Termination (Cost-Reimbursement)
52.249-14	Apr 1984	Excusable Delays

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CFR CHAPTER 3) CLAUSES

HHSAR Clause No.	Date	Title
352.202-1	Jan 2001	Definitions - with Alternate paragraph (h) (Jan 2001)
352.228-7	Dec 1991	Insurance - Liability to Third Persons
352.232-9	Apr 1984	Withholding of Contract Payments
352.233-70	Apr 1984	Litigation and Claims
352.242-71	Apr 1984	Final Decisions on Audit Findings
352.270-5	Apr 1984	Key Personnel
352.270-6	Jul 1991	Publication and Publicity

ARTICLE I.2. AUTHORIZED SUBSTITUTIONS OF CLAUSES

Any authorized substitutions and/or modifications other than the General Clauses which will be based on the type of contract/Contractor will be determined during negotiations.

It is expected that the following clause(s) will be made part of the resultant contract:

FAR Clause 52.232-20, LIMITATION OF COST, is deleted in its entirety and FAR Clause 52.232-22, LIMITATION OF FUNDS (APRIL 1984) is substituted therefor. **[Note: When this contract is fully funded, FAR Clause 52.232-22, LIMITATION OF FUNDS will no longer apply and FAR Clause 52.232-20, LIMITATION OF COST will become applicable.**

ARTICLE I.3. ADDITIONAL CONTRACT CLAUSES

Additional clauses other than those listed below which are based on the type of contract/Contractor shall be determined during negotiations. Any contract awarded from this solicitation will contain the following:

This contract incorporates the following clauses by reference, (unless otherwise noted), with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available.

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CFR CHAPTER 1) CLAUSES

FAR 52.217-8, Option to Extend Services (NOVEMBER 1999).

"...The Contracting Officer may exercise the option by written notice to the Contractor within the five-year contract period.

FAR 52.217-9, Option to Extend the Term of the Contract (MARCH 2000).

"(a) The Government may extend the term of this contract by written notice to the Contractor within [INSERT THE PERIOD OF TIME WITHIN WHICH THE CONTRACTING OFFICER MAY EXERCISE THE OPTION] ; provided that the Government gives the Contractor a preliminary written notice of its intent to extend at least 60 days before the contract expires. The preliminary notice does not commit the Government to an extension."

(c) The total duration of this contract, including the exercise of any options under this clause, shall not exceed September 2010.

FAR 52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns (MAY 2001).

"(b) Evaluation adjustment. (1) The Contracting Officer will evaluate offers by adding a factor of 10 percent to the price of all offers, except--..."

FAR 52.227-14, Rights in Data - General (JUNE 1987)

Alternate III (JUNE 1987), FAR 52.227-14, Rights in Data--General (JUNE 1987).

Additions to, or limitations on, the restricted rights set forth in the Restricted Rights Notice of subparagraph (g)(3) of the clause are expressly stated as follows:

FAR 52.227-16, Additional Data Requirements (JUNE 1987).

FAR 52.227-17, Rights in Data--Special Works (JUNE 1987).

FAR 52.227-18, Rights in Data--Existing Works (JUNE 1987).

FAR 52.227-19, Commercial Computer Software--Restricted Rights (JUNE 1987).

FAR 52.230-2, Cost Accounting Standards (APRIL 1998).

FAR 52.230-3, Disclosure and Consistency of Cost Accounting Practices (APRIL 1998).

FAR 52.230-6, Administration of Cost Accounting Standards (NOVEMBER 1999).

FAR 52.237-3, Continuity of Services (JANUARY 1991).

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION/PUBLIC HEALTH SERVICE ACQUISITION REGULATION (HHSAR)/(PHSAR) (48 CHAPTER 3) CLAUSES:

c. NATIONAL INSTITUTES OF HEALTH (NIH) RESEARCH CONTRACTING (RC) CLAUSES:

The following clauses are attached and made a part of this contract:

NIH (RC)-7, Procurement of Certain Equipment (APRIL 1984) (OMB Bulletin 81-16).

ARTICLE I.4. ADDITIONAL FAR CONTRACT CLAUSES INCLUDED IN FULL TEXT

Additional clauses other than those listed below which are based on the type of contract/Contractor shall be determined during negotiations. Any contract awarded from this solicitation will contain the following:

This contract incorporates the following clauses in full text.

FEDERAL ACQUISITION REGULATION (FAR)(48 CFR CHAPTER 1) CLAUSES:

FAR Clause 52.244-6, SUBCONTRACTS FOR COMMERCIAL ITEMS (MAY 2002)

(a) **Definitions**. As used in this clause--

Commercial item, has the meaning contained in the clause at 52.202-1, Definitions.

Subcontract, includes a transfer of commercial items between divisions, subsidiaries, or affiliates of the Contractor or subcontractor at any tier.

(b) To the maximum extent practicable, the Contractor shall incorporate, and require its subcontractors at all tiers to incorporate, commercial items or nondevelopmental items as components of items to be supplied under this contract.

(c) (1) The Contractor shall insert the following clauses in subcontracts for commercial items:

(i) 52.219-8, Utilization of Small Business Concerns (OCT 2000) (15 U.S.C. 637(d)(2) and (3)), in all subcontracts that offer further subcontracting opportunities. If the subcontract (except subcontracts to small business concerns) exceeds $500,000 ($1,000,000 for construction of any public facility), the subcontractor must include 52.219-8 in lower tier subcontracts that offer subcontracting opportunities.
(ii) 52.222-26, Equal Opportunity (APR 2002) (E.O. 11246).
(iii) 52.222-35, Equal Opportunity for Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans (DEC 2001) (38 U.S.C. 4212(a)).
(iv) 52.222-36, Affirmative Action for Workers with Disabilities (JUN 1998) (29 U.S.C. 793).
(v) 52.247-64, Preference for Privately Owned U.S.-Flag Commercial Vessels (JUN 2000) (46 U.S.C. Appx 1241) (flowdown not required for subcontracts awarded beginning May 1, 1996).

(2) While not required, the Contractor may flow down to subcontracts for commercial items a minimal number of additional clauses necessary to satisfy its contractual obligations.

(d) The Contractor shall include the terms of this clause, including this paragraph (d), in subcontracts awarded under this contract.

52.246-24 Limitation of Liability-High-Value Items.

As prescribed in 46.805, insert the following clause:

Limitation of Liability-High-Value Items (Feb 1997)

If the contract is for both high-value items and other end items, the contracting officer shall identify the high-value items by line item and insert the following preamble before paragraph (a): Source Codes

a) Except as provided in paragraphs (b) through (e) of this clause, and notwithstanding any other provision of this contract, the Contractor shall not be liable for loss of or damage to property of the Government (including the supplies delivered under this contract) that-
(1) Occurs after Government acceptance of the supplies delivered under this contract; and
(2) Results from any defects or deficiencies in the supplies.
(b) The limitation of liability under paragraph (a) of this clause shall not apply when a defect or deficiency in, or the Government's acceptance of, the supplies results from willful misconduct or lack of good faith on the part of any of the Contractor's managerial personnel. The term "Contractor's managerial personnel," as used in this clause, means the

Contractor's directors, officers, and any of the Contractor's managers, superintendents, or equivalent representatives who have supervision or direction of-

(1) All or substantially all of the Contractor's business;

(2) All or substantially all of the Contractor's operations at any one plant, laboratory, or separate location at which the contract is being performed; or

(3) A separate and complete major industrial operation connected with the performance of this contract.

(c) If the Contractor carries insurance, or has established a reserve for self-insurance, covering liability for loss or damage suffered by the Government through purchase or use of the supplies required to be delivered under this contract, the Contractor shall be liable to the Government, to the extent of such insurance or reserve, for loss of or damage to property of the Government occurring after Government acceptance of, and resulting from any defects or deficiencies in, the supplies delivered under this contract.

(d)(1) This clause does not diminish the Contractor's obligations, to the extent that they arise otherwise under this contract, relating to correction, repair, replacement, or other relief for any defect or deficiency in supplies delivered under this contract.

(2) Unless this is a cost-reimbursement contract, if loss or damage occurs and correction, repair, or replacement is not feasible or desired by the Government, the Contractor shall, as determined by the Contracting Officer-

(i) Pay the Government the amount it would have cost the Contractor to make correction, repair, or replacement before the loss or damage occurred;

(ii) Provide other equitable relief.

(e) This clause shall not limit or otherwise affect the Government's rights under clauses, if included in this contract, that cover-

(1) Warranty of technical data;

(2) Ground and flight risks or aircraft flight risks; or

(3) Government property.

PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

SECTION J - LIST OF ATTACHMENTS

The following Attachments are provided in full text with this Solicitation:

PACKAGING AND DELIVERY OF PROPOSALS (Attached to this listing)

HOW TO PREPARE AN ELECTRONIC PROPOSAL: (Attached to this listing)

PROPOSAL INTENT RESPONSE SHEET [SUBMIT ON/BEFORE: October 15, 2002. (Attached to this listing)

[NOTE: Your attention is directed to the "Proposal Intent Response Sheet". If you intend to submit a proposal, you must complete this form and return it to this office via fax or e-mail on or before the date identified above. The receipt of this form is critical as it contains information essential for CMB's coordination of the electronic submission and review of proposals.]

RFP FORMS AND ATTACHMENTS:

THE RFP FORMS/ATTACHMENTS LISTED BELOW ARE AVAILABLE IN A VARIETY OF FORMATS AND MAY BE VIEWED OR DOWNLOADED DIRECTLY FROM THIS SITE:

http://www.niaid.nih.gov/contract/ref.htm

APPLICABLE TO TECHNICAL PROPOSAL (INCLUDE THESE DOCUMENTS/FORMS WITH YOUR TECHNICAL PROPOSAL):

Technical Proposal Cost Information
Summary of Related Activities
Government Notice for Handling Proposals

APPLICABLE TO BUSINESS PROPOSAL (INCLUDE WITH YOUR BUSINESS PROPOSAL):

NIH-2043, Proposal Summary and Data Record
Small Business Subcontracting Plan Format *[if applicable]*
Breakdown of Proposed Estimated Cost (plus fee) and Labor Hours
Offeror's Points of Contact

TO BECOME CONTRACT ATTACHMENTS (INFORMATION ONLY):

NIH(RC)-4: Invoice/Financing Request and Contract Financial Reporting Instructions for NIH Cost-Reimbursement Type Contracts
NIH(RC)-7: Procurement of Certain Equipment, (OMB Bulletin 81-16)
Privacy Act System of Records
Report of Government Owned, Contractor Held Property
Government Property – Schedule ___
Disclosure of Lobbying Activities, OMB Form LLL

PACKAGING/DELIVERY/ELECTRONIC SUBMISSION OF THE PROPOSAL

Listed below are delivery instructions for the submission of both PAPER and ELECTRONIC COPIES of your proposal.

PAPER SUBMISSION: *The paper copy is the official copy for recording timely receipt of proposals.* You are required to submit one original paper copy of your proposal along with the number of extra copies required below.

ELECTRONIC SUBMISSION: In addition to the paper submission, you are required to submit your proposal electronically through the CRON (Contracts Review Online) in accordance with the instructions provided below. If you experience difficulty or are unable to transmit, you should submit your proposal on a CD-Rom or ZipDisk by an express delivery service. We can then upload your proposal into the electronic system. You must certify that both the original paper and electronic versions of the proposal are identical.

SUBMISSION OF PROPOSALS BY FACSIMILE IS NOT ACCEPTABLE.

Shipment and marking of paper copies shall be as indicated below:

A. EXTERNAL PACKAGE MARKING:

In addition to the address cited below, mark each package as follows:

"RFP NO. NIH-NIAID-03-31 TO BE OPENED BY AUTHORIZED GOVERNMENT PERSONNEL ONLY"

B. NUMBER OF COPIES:

The number of copies required of each part of your proposal are as specified below.

Technical Proposal: One (1) unbound signed original and five (5) unbound copies. Ten (10) copies of all material not available electronically (i.e. SOPs, Pertinent Manuals, Nonscannable Figures or Data, and Letters of Collaboration/Intent).

Business Proposal: One (1) unbound signed original and 5 unbound copies.

C. PAPER COPIES and CD-Rom or ZipDisk to:

If Hand Delivery or Express Service	If using U.S. Postal Service
Suzanne L. Dawkins Contract Specialist Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230 Bethesda, Maryland 20817	Suzanne L. Dawkins Contract Specialist Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230, MSC 7612 Bethesda, Maryland 20892-7612

NOTE: All material sent to this office by Federal Express should be sent to the Hand Carried Address.

NOTE: The U.S. Postal Service's "Express Mail" does not deliver to the hand delivered (20817 zip code) address. Any package sent to this address via this service will be held at a local post office for pick-up. THE GOVERNMENT IS NOT RESPONSIBLE FOR PICKING UP ANY MAIL AT A LOCAL POST OFFICE. If a proposal is not received at the place, date, and time specified herein, it will be considered a "late proposal," in accordance with HHSAR 352.215-70, Late Proposals and Revisions (NOV 1986).

HOW TO PREPARE AND SUBMIT AN ELECTRONIC PROPOSAL

PAGE LIMITS -- THE TECHNICAL PROPOSAL IS LIMITED TO NOT-TO-EXCEED 200 PAGES INCLUDING: Appendices, Attachments, Graphics, Tables, Figures, Operating Manuals, Non-Scannable Figures or Data, Letters of Intent, etc. In addition to the 200 page limitation, CVs are limited to 3 pages per person and reprints are limited to 10 pages for the entire project. As with the technical proposal, the CV and reprint section is limited to not-to-exceed 200 pages. ANY PORTIONS OF YOUR PROPOSAL NOT AVAILABLE ELECTRONICALLY ARE ALSO CONSIDERED TO BE INCLUDED IN THE TOTAL PAGE LIMITATION. PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE PROPOSAL AND WILL NOT BE READ OR EVALUATED.

Note that although no page limit has been placed on the Business Proposal, offerors are encouraged to limit its content to only those documents necessary to provide adequate support for the proposed costs.

ELECTRONIC SUBMISSION – To submit a proposal electronically under this RFP, offerors will need to prepare the proposal on a word processor or spreadsheet program (for the business portion) and convert them to Adobe Acrobat Portable Document Format (.pdf). THE TECHNICAL PROPOSAL AND BUSINESS PROPOSAL MUST BE CONTAINED ON SEPARATE FILES which must be identified as either TECHNICAL or BUSINESS and include some recognizable portion of the ORGANIZATION NAME.

Please note that the electronic submission does not replace the requirement to submit a signed, unbound original paper copy of both your Technical and Business Proposal, along with any required unbound duplicate copies. These paper originals should be mailed or hand-delivered to the address provided in this attachment and must be received on/before the closing date and time.

There is no limit to the size (MB) of the two electronic PDF files to be submitted; however, the size of the technical proposal is limited to the page limitation language outlined above. For purposes of assessing compliance with the page count, technical proposals will be viewed using the print function of the Adobe Acrobat Reader, Version 4.0 (or higher).

Formatting Requirements:

- Do not embed sound or video (e.g., MPEG) files into the proposal documents. The evaluation system does not have the capability to read these files.
- Keep graphics embedded in documents as simple as possible. Complex graphics require longer periods for the computers used in the evaluation system to draw, and redraw these figures and scrolling through the document is slowed significantly.
- Type density and size must be 10 to 12 points. If constant spacing is used, there should be no more than 15 cpi, whereas proportional spacing should provide an average of no more than 15 cpi. There must be no more than six lines of text within a vertical inch. Margins must be set to 1 inch around.
- Paper size should not exceed 8-1/2 x 11. Larger paper sizes will be counted as 2 pages.
- Limit colors to 256 colors at 1024 x 768 resolution; avoid color gradients.
- Simplify the color palette used in creating figures.
- Be aware of how large these graphics files become. Large files are discouraged.
- Limit scanned images as much as possible.
- Limit appendices and attachments to relevant technical proposal information (e.g., SOPs, pertinent manuals, non-scannable figures or data, resumes, letters of commitment/intent).

SUBMISSION OF "PROPOSAL INTENT TO RESPOND SHEET":

Upon receipt by the Contracting Officer of the "Proposal Intent Response Sheet", offerors will be provided, via e-mail correspondence, specific electronic access information and electronic proposal transmission instructions. For this reason, it is imperative that all offerors who are intending to submit a proposal in response to this RFP contact the Contract Specialist identified in this RFP and complete and submit the attached "Proposal Intent Response Sheet" by the date provided on that Attachment.

CREATE ADOBE PDF ONLINE -- Adobe will allow you to create 5 documents on a trial for free. If you want to use the site regularly it costs $10/month or $100/year. Please link to the following URL for information:

https://createpdf.adobe.com/index.pl/3847995518.39272?BP=IE

LOG-IN / TRANSMISSION INSTRUCTIONS:

1. Log-in Site: Will be provided by the Contract Specialist after receipt of the "Proposal Intent Response Sheet"
2. Log-in Name: Will be provided by the Contract Specialist.
3. Log-in Password: Will be provided by the Contract Specialist.

4. Procedure -- When your proposal is completed and converted to a PDF file using Adobe Acrobat, it is ready to be transmitted electronically. You must upload separate Technical and Business Proposal Files. It is recommended that proposals be transmitted a few days before the due date so that you will have sufficient time to overcome any transmission difficulties.

- You must have Explorer 3.1 or higher.
- It is essential that you use antiviral software to scan all documents.
- Click on "Sign On" and enter your log-in name and password.
- Click on "Browse" to locate your saved files on your computer.
- Click on "Upload Proposal" after you have located the correct file.
- After a file is uploaded, a link to the file will appear under "Upload Files" at the bottom of the screen. Click on that link to view the uploaded file.
- If you experience difficulty in accessing your documents, please contact the appropriate NIH contracts office immediately.
- If you wish to revise your proposal before the closing date and time, simply log in again and re-post.

4. **USER ACCESS TO THE POSTING SITE WILL BE DENIED AFTER THE RFP CLOSING DATE AND TIME PROVIDED WITH THIS RFP OR ITS MOST RECENT AMENDMENT(S).**

PROPOSAL INTENT RESPONSE SHEET

RFP No.: NIH-NIAID-03-31
RFP Title: "Immune Epitope Database and Analysis Program"

Please review the attached Request for Proposal. Furnish the information requested below and return this page by October 15, 2002. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

Since your proposal will be submitted electronically, please include the name and e-mail of the individual to whom the electronic proposal instructions, login code, and password should be provided.

[ ] DO INTEND TO SUBMIT A PROPOSAL
[ ] DO NOT INTEND TO SUBMIT A PROPOSAL FOR THE FOLLOWING REASONS:

Company/Institution Name (print): _____
Address (print): _____
_____
_____
_____

Project Director's Name (print): _____
Title (print): _____
Signature/Date: _____
Telephone Number and E-mail Address (print clearly):
_____
_____

***Name of individual to whom electronic proposal instructions should be sent:**

Name: _____
Title: _____
E-Mail Address: _____
Telephone Number: _____

Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):

_____
_____
_____
_____
(Continue list on a separate page if necessary)

RETURN VIA FAX OR E-MAIL TO:
CMB, NIAID, NIH
Room 2230
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn: Suzanne L. Dawkins
RFP-NIH-NIAID-03-31
Phone # (301) 496-0612
FAX # (301) 402-0972
Email : sd33r@nih.gov

PART IV – REPRESENTATIONS AND INSTRUCTIONS

SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

Representations, Certifications, and Other Statements of Offerors or Quoters (Negotiated).

1. REPRESENTATIONS AND CERTIFICATIONS

The Representations and Certifications required by this particular acquisition can be accessed electronically from the INTERNET at the following address:

http://rcb.cancer.gov/rcb-internet/forms/rcneg.pdf

If you are unable to access this document electronically, you may request a copy from the Contracting Officer identified on the cover page of this solicitation.

IF YOU INTEND TO SUBMIT A PROPOSAL, YOU MUST COMPLETE THE REPRESENTATIONS AND CERTIFICATIONS AND SUBMIT THEM AS PART OF YOUR BUSINESS PROPOSAL.

SECTION L - INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS

1. GENERAL INFORMATION

Alternate I (October 1997). As prescribed in 15.209(a)(1), substitute the following paragraph (f)(4) for paragraph (f)(4) of the basic provision:

> (f) (4) The Government intends to evaluate proposals and award a contract after conducting discussions with offerors whose proposals have been determined to be within the competitive range. If the Contracting Officer determines that the number of proposals that would otherwise be in the competitive range exceeds the number at which an efficient competition can be conducted, the Contracting Officer may limit the number of proposals in the competitive range to the greatest number that will permit an efficient competition among the most highly rated proposals. Therefore, the offeror's initial proposal should contain the offeror's best terms from a price and technical standpoint.

a. **NAICS CODE AND SIZE STANDARD**

Note: The following information is to be used by the offeror in preparing its Representations and Certifications (See Section K of this RFP), specifically in completing the provision entitled, SMALL BUSINESS PROGRAM REPRESENTATION, FAR Clause 52.219-1.

(1) The North American Industry Classification System (NAICS) code for this acquisition is 541710.
(2) The small business size standard is 500 employees.

5. **THIS REQUIREMENT IS NOT SET-ASIDE FOR SMALL BUSINESS. However, the Federal Acquisition Regulation (FAR) requires in every solicitation, (except for foreign acquisitions) the inclusion of the North American Industry Classification System (NAICS) Code and corresponding size standard which best describes the nature of the requirement in the solicitation.**

b. **NOTICE OF PRICE EVALUATION ADJUSTMENT FOR SMALL DISADVANTAGED BUSINESS CONCERNS**

In accordance with FAR Clause 52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns, incorporated in Section I.3., offerors will be evaluated by adding a factor of ten percent to the price of all offers, except offers from small disadvantaged business concerns that have not waived the adjustment. (Note: A listing of other offerors who are excepted and will not have this evaluation factor added to their offer may be found in subparagraph (b) of FAR Clause 52.219-23.

A small disadvantaged business concern may elect to waive the adjustment, in which case the factor will be added to its offer for evaluation purposes. The agreements in paragraph (d) of FAR Clause 52.219-23 do not apply to offerors that waive the adjustment.

6. **AN OFFEROR WHO ELECTS TO WAIVE THIS EVALUATION ADJUSTMENT MUST SPECIFICALLY INDICATE WITH A STATEMENT TO THIS EFFECT ON THE COVER PAGE OF ITS BUSINESS PROPOSAL.**

c. **TYPE OF CONTRACT AND NUMBER OF AWARD(S)**

It is anticipated that one award will be made from this solicitation and that the award will be made on/about November 26, 2002.

It is anticipated that the award from this solicitation will be a multiple-year cost reimbursement type completion contract with a period of performance of five years with 2 one-year option periods and that incremental funding will be used [see Section L.2.c. Business Proposal Instructions].

d. **ESTIMATE OF EFFORT**

It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the five year total effort to be approximately 8,350% labor hours (1,670% per year) or 11,690% if the two option years are exercised. This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

Estimated Level of Effort (% Time Per Year)

Position	Percent Effort per Year
Principal Investigator	20
System Analyst (General Project Lead)	100
Senior Scientist (Immunology Group Lead)	100
Database Designer	100
Program Analysts	
2 Level IV Programmers (or Software Engineers)	100
2 Level III Programmers	100
Scientists (4)	100
Web Designer	100
Database Administration	25
Web Administrator	25
Quality Assurance/Tester (2)	100
Data Entry Support (4)	100
TOTAL	1,670 per year

The Government estimates that the performance of the activities presented in the Statement of Work will require a dedicated database server, a dedicated web serve, substantial personnel including the Principal Investigator, System Analyst (Project Lead), Senior Scientist/Immunology Group lead (data annotation and curation), Database Designer, Web Designer, Program Analysts (programmers), Scientists (data annotation and curation), quality Assurance/Testers, Database Administrator, and Web Administrator. These estimates are for the Contractors' information only and are not to be considered restrictive for proposal purposes. The Government's estimate of the level of effort required for this RFP is included for guidance only in SECTION L – INSTRUCTIONS, CONDITIONS AND NOTICES TO OFFERORS – Paragraph d. ESTIMATE OF EFFORT. This estimate, also, in Section L is not considered restrictive for proposal purposes.

e. **COMMITMENT OF PUBLIC FUNDS**

The Contracting Officer is the only individual who can legally commit the Government to the expenditure of public funds in connection with the proposed procurement. Any other commitment, either explicit or implied, is invalid.

f. **COMMUNICATIONS PRIOR TO CONTRACT AWARD**

Offerors shall direct all communications to the attention of the Contract Specialist or Contracting Officer cited on the face page of this RFP. Communications with other officials may compromise the competitiveness of this acquisition and result in cancellation of the requirement.

g. **RELEASE OF INFORMATION**

Contract selection and award information will be disclosed to offerors in accordance with regulations applicable to negotiated acquisition. Prompt written notice will be given to unsuccessful offerors as they are eliminated from the competition, and to all offerors following award.

h. **COMPARATIVE IMPORTANCE OF PROPOSALS**

You are advised that paramount consideration shall be given to the evaluation of technical proposals. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. The relative importance of the evaluation factors is specified in SECTION M of this solicitation. However, the Government reserves the right to make an award to the best advantage of the Government, cost and other factors considered.

i. **PREPARATION COSTS**

This RFP does not commit the Government to pay for the preparation and submission of a proposal.

j. **SERVICE OF PROTEST** (AUGUST 1996) - FAR 52.233-2

(a) Protests, as defined in section 33.101 of the Federal Acquisition Regulation, that are filed directly with an agency, and copies of any protests that are filed with the General Accounting Office (GAO), shall be served on the Contracting Officer (addressed as follows) by obtaining written and dated acknowledgment of receipt from:

Brenda J. Velez
Contracting Officer
Contract Management Branch, DEA
National Institute of Allergy and Infectious Diseases
6700-B Rockledge Drive, Room 2230, MSC 7612
BETHESDA MD 20892-7612

(b) The copy of any protest shall be received in the office designated above within one day of filing a protest with the GAO.

k. **AVAILABILITY OF THE "FEDERAL ADP AND TELECOMMUNICATIONS STANDARDS INDEX."**

Copies of the "Federal ADP and Telecommunications Standards Index" can be purchased from the U.S. Government Printing Office, Superintendent of Documents, Washington, DC 20402.

l. **USE OF INTERNET WEB SITE ADDRESSES (URLs) IN PROPOSALS**

Unless otherwise specified or required in NIAID solicitations, internet Web Site addresses (URLs) may not be used to provide information necessary to the conduct of the review of the proposal. Direct access to an internet site by a Reviewer who is examining and reviewing the proposal on behalf of the NIAID could compromise their anonymity during the review process. If a URL contains information pertinent to the proposal content, the offeror must provide access to the website via a temporary website portal which allow reviewers the capability to view and interact with the site.

The proposal must clearly identify the URLs to be accessed and the procedure for accessing the temporary website portal. Access must not require the identity of the individual.

INSTRUCTIONS TO OFFERORS

GENERAL INSTRUCTIONS

INTRODUCTION

The following instructions will establish the acceptable minimum requirements for the format and contents of proposals. Special attention is directed to the requirements for technical and business proposals to be submitted in accordance with these instructions.

(1) **Contract Type and General Clauses**

It is contemplated that a cost-reimbursement (completion) type contract will be awarded. (See General Information) Any resultant contract shall include the clauses applicable to the selected offeror's organization and type of contract awarded as required by Public Law, Executive Order, or acquisition regulations in effect at the time of execution of the proposed contract.

(2) **Authorized Official and Submission of Proposal**

The proposal must be signed by an official authorized to bind your organization and must stipulate that it is predicated upon all the terms and conditions of this RFP. Your proposal shall be submitted in the number of copies, to the addressees, and marked as indicated in the Attachment entitled, PACKAGING AND DELIVERY OF PROPOSAL, Part III, Section J hereof. Proposals will be typewritten, paginated, reproduced on letter size paper and will be legible in all required copies. To expedite the proposal evaluation, all documents required for responding to the RFP should be placed in the following order:

I. COVER PAGE

Include RFP title, number, name of organization, identification of the proposal part, and indicate whether the proposal is an original or a copy.

II. TECHNICAL PROPOSAL

It is recommended that the technical proposal consist of a cover page, a table of contents, and the information requested in the Technical Proposal Instructions and as specified in SECTION J, List of Attachments.

III. BUSINESS PROPOSAL

It is recommended that the business proposal consist of a cover page, a table of contents, and the information requested in the Business Proposal Instructions and as specified in SECTION J, List of Attachments.

(3) **Proposal Summary and Data Record (NIH-2043)**

The Offeror must complete the Form NIH-2043, attached, with particular attention to the length of time the proposal is firm and the designation of those personnel authorized to conduct negotiations. (See Section J, Attachment entitled, PROPOSAL SUMMARY AND DATA RECORD).

(4) **Separation of Technical and Business Proposals**

The proposal must be prepared in two parts: a "Technical Proposal" and a "Business Proposal." Each of the parts shall be separate and complete in itself so that evaluation of one may be accomplished independently of, and concurrently with, evaluation of the other. The technical proposal must include direct cost and resources information, such as labor-hours and categories and applicable rates, materials, subcontracts, travel, etc., and associated costs so that the offeror's understanding of the project may be evaluated (See Attachment entitled, TECHNICAL PROPOSAL COST INFORMATION/SUMMARY OF LABOR AND DIRECT COSTS).) However,

the technical proposal should **not** include pricing data relating to individual salary information, indirect cost rates or amounts, fee amounts (if any)., and total costs. The technical proposal should disclose your technical approach in as much detail as possible, including, but not limited to, the requirements of the technical proposal instructions.

(5) **Alternate Proposals**

You may, at your discretion, submit alternate proposals, or proposals which deviate from the requirements; provided, that you also submit a proposal for performance of the work as specified in the statement of work. Such proposals may be considered if overall performance would be improved or not compromised and if they are in the best interests of the Government. Alternative proposals, or deviations from any requirements of this RFP, shall be clearly identified.

(6) **Evaluation of Proposals**

The Government will evaluate technical proposals in accordance with the criteria set forth in PART IV, SECTION M of this RFP.

(7) **Potential Award Without Discussions**

The Government reserves the right to award a contract without discussions if the Contracting Officer determines that the initial prices are fair and reasonable and that discussions are not necessary.

(8) **Use of the Metric System of Measurement**

It is the policy of the Department of Health and Human Services to support the Federal transition to the metric system and to use the metric system of measurement in all procurements, grants, and other business related activities unless such use is impracticable or is likely to cause significant inefficiencies.

The offeror is encouraged to prepare their proposal using either "Hard Metric," "Soft Metric," or "Dual Systems" of measurement. The following definitions are provided for your information:

Hard Metric - The replacement of a standard inch-pound size with an accepted metric size for a particular purpose. An example of size substitution might be: selling or packaging liquids by the liter instead of by the pint or quart (as for soft drinks), or instead of by the gallon (as for gasoline).

Soft Metric - The result of a mathematical conversion of inch-pound measurements to metric equivalents for a particular purpose. The physical characteristics are not changed.

Dual Systems - The use of both inch-pound and metric systems. For example, an item is designed, produced, and described in inch-pound values with soft metric values also shown for information or comparison purposes.

(9) **Obtaining and Disseminating Biomedical Research Resources**

As a public sponsor of biomedical research, the National Institutes of Health (NIH) has a dual interest in accelerating scientific discovery and facilitating product development. Intellectual property restrictions can stifle the broad dissemination of new discoveries and limit future avenues of research and product development. At the same time, reasonable restrictions on the dissemination of research tools are sometimes necessary to protect legitimate proprietary interests and to preserve incentives for commercial development. To assist NIH contractors achieve an appropriate balance, the NIH has provided guidance in the form of a two-part document, consisting of Principles setting forth the fundamental concepts and Guidelines that provide specific information to patent and license professionals and sponsored research administrators for implementation.

The purpose of these Principles and Guidelines is to assist NIH funding recipients in determining: 1) Reasonable terms and conditions for making NIH-funded research resources available to scientists in other institutions in the public and private sectors (disseminating research tools); and 2) Restrictions to accept as a conditions of receiving

access to research tools for use in NIH-funded research (acquiring research tools). The intent is to help recipients ensure that the conditions they impose and accept on the transfer of research tools will facilitate further biomedical research, consistent with the requirements of the Bayh-Dole Act and NIH funding policy.

This policy, entitled, "Sharing Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts," (Federal Register Notice, December 23, 1999 [64 FR 72090] will be included in any contract awarded from this solicitation. It can be found at the following website: http://ott.od.nih.gov/NewPages/64FR72090.pdf.

(10) **Privacy Act (Treatment of Proposal Information)**

The Privacy Act of 1974 (P.L. 93-579) requires that a Federal agency advise each individual whom it asks to supply information, the authority which authorizes the solicitation, whether disclosure is voluntary or mandatory, the principal purpose or purposes for which the information is intended to be used, the uses outside the agency which may be made of the information, and the effects on the individual, if any, of not providing all or any part of the requested information.

The NIH is requesting the information called for in this RFP pursuant to the authority provided by Sec. 301(a)(7) of the Public Health Service Act, as amended, and P.L. 92-218, as amended.

Providing the information requested is entirely voluntary. The collection of this information is for the purpose of conducting an accurate, fair, and adequate review prior to a discussion as to whether to award a contract.

Failure to provide any or all of the requested information may result in a less than adequate review.

In addition, the Privacy Act of 1974 (P.L. 93-579, Section 7) requires that the following information be provided when individuals are requested to disclose their social security number.

Provision of the social security number is voluntary. Social security numbers are requested for the purpose of accurate and efficient identification, referral, review and management of NIH contracting programs. Authority for requesting this information is provided by Section 301 and Title IV of the PHS Act, as amended.

The information provided by you may be routinely disclosed for the following purposes:

- to the cognizant audit agency and the General Accounting Office for auditing.
- to the Department of Justice as required for litigation.
- to respond to congressional inquiries.
- to qualified experts, not within the definition of Department employees, for opinions as a part of the review process.

(11) **Selection of Offerors**

a) The acceptability of the scientific and technical portion of each research contract proposal will be evaluated by a technical review committee. The committee will evaluate each proposal in strict conformity with the evaluation criteria of the RFP, utilizing point scores and written critiques. The committee may suggest that the Contracting Officer request clarifying information from an offeror.

b) The business portion of each contract proposal will be subjected to a cost and price analysis, management analysis, etc.

c) If award will be made without conducting discussions, offerors may be given the opportunity to clarify certain aspects of their proposal (e.g., the relevance of an offeror's past performance information and adverse past performance information to which the offeror has not previously had an opportunity to respond) or to resolve minor or clerical errors.

d) If the Government intends to conduct discussions prior to awarding a contract-

(1) Communications will be held with offerors whose past performance information is the determining factor preventing them from being placed within the competitive range. Such communications shall address adverse past performance information to which an offeror has not had a prior opportunity to respond. Also, communications may be held with any other offerors whose exclusion from, or inclusion in, the competitive range is uncertain.

Such communications shall not be used to cure proposal deficiencies or omissions that alter the technical or cost elements of the proposal, and/or otherwise revise the proposal, but may be considered in rating proposals for the purpose of establishing the competitive range.

(2) The Contracting Officer will, in concert with program staff, decide which proposals are in the competitive range. The competitive range will be comprised of all of the most highly rated proposals. Oral or written discussions will be conducted with all offerors in the competitive range.

While it is this Institute's policy to conduct discussions with all offerors in the competitive range, the Institute reserves the right, in special circumstances, to limit the number of proposals included in the competitive range to the greatest number that will permit an efficient competition. All aspects of the proposals are subject to discussions, including cost, technical approach, past performance, and contractual terms and conditions. At the conclusion of discussions, each offeror still in the competitive range shall be given an opportunity to submit a written Final Proposal Revision (FPR) with the reservation of the right to conduct finalization of details with the selected sources in accordance with HHSAR 315.370.

e) The process described in FAR 15.101-1 will be employed, which permits the Government to make tradeoffs among cost or price and non-cost factors and to consider award to other than the lowest price offeror or other than the highest technically rated offeror. This process will take into consideration the results of the technical evaluation, the past performance evaluation (if applicable) and the cost analysis.

f) The Institute reserves the right to make a single award, multiple awards, or no award at all to the RFP. In addition, the RFP may be amended or canceled as necessary to meet the Institute's requirements. Synopses of awards exceeding $25,000 will be published in the Commerce Business Daily and FedBizOpps.

(12) **Small Business Subcontracting Plan**

If the proposed contract exceeds a total estimated cost of $500,000 for the entire period of performance, the offeror shall be required to submit an acceptable subcontracting plan in accordance with the terms of the clause entitled "Small Business Subcontracting Plan," FAR Clause No. 52.219-9, incorporated herein by reference in the Solicitation, Attachment _ to this RFP is an example of such a plan.

a) THIS PROVISION DOES NOT APPLY TO SMALL BUSINESS CONCERNS.

b) The term "subcontract" means any agreement (other than one involving an employer-employee relationship) entered into by a Federal Government prime Contractor or subcontractor calling for supplies or services required for the performance of the original contract or subcontract. This includes, but is not limited to, agreements/purchase orders for supplies and services such as equipment purchase, copying services, and travel services.

c) The offeror understands that:

(1) No contract will be awarded unless and until an acceptable plan is negotiated with the Contracting Officer which plan will be incorporated into the contract, as a material part thereof.

(2) An acceptable plan must, in the determination of the Contracting Officer, provide the maximum practicable opportunity for Small Businesses, Small Disadvantaged Businesses, Women-Owned Small businesses, HubZone Small Businesses, Veteran-Owned Small Businesses, and Service Disabled Veteran-Owned Small Businesses to participate in the performance of the contract.

(3) If a subcontracting plan acceptable to the Contracting Officer is not negotiated within the time limits prescribed by the contracting activity and such failure arises out of causes within the control and with the fault or negligence of the offeror, the offeror shall be ineligible for an award. The Contracting Officer shall notify the Contractor in writing of the reasons for determining a subcontracting plan unacceptable early enough in the negotiation process to allow the Contractor to modify the plan within the time limits prescribed.

(4) Prior compliance of the offeror with other such subcontracting plans under previous contracts will be considered by the Contracting Officer in determining the responsibility of the offeror for award of the contract.

(5) It is the offeror's responsibility to develop a satisfactory subcontracting plan with respect to Small Business Concerns, Small Disadvantaged Business Concerns, Women-Owned Small Business Concerns, HubZone Small Business Concerns, Veteran-Owned Small Business Concerns, and Service Disabled Veteran-Owned Small Business Concerns that each such aspect of the offeror's plan will be judged independent of the other.

(5) The offeror will submit, as required by the Contracting Officer, subcontracting reports in accordance with the instructions thereon, and as further directed by the Contracting Officer. Subcontractors will also submit these reports to the Government's Contracting Officer or as otherwise directed, with a copy to the prime Contractor's designated small and disadvantaged business liaison.

b) Each plan must contain the following:

(1) Goals, expressed in terms of percentages of total planned subcontracting dollars, for the use of Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Business Concerns as subcontractors.

(2) A statement of total dollars planned to be subcontracted. A statement of total dollars to be subcontracted to each of the following type of small business concerns: Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses.

(3) A description of the principal types of supplies and services to be subcontracted with an identification of which supplies and services are expected to be subcontracted to Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned and/or Service Disabled Veteran-Owned Small Business Concerns.

(4) A description of the method used to develop the subcontracting goals.

(5) A description of the method used to identify potential sources for solicitation purposes.

(6) A statement as to whether or not indirect costs were included in establishing subcontracting goals. If they were, a description of the method used to determine the proportionate share of indirect costs to be incurred with Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses.

(7) The name of the individual employed by the offeror who will administer the offeror's subcontracting program and a description of his/her duties.

(8) A description of the efforts the offeror will make to assure that Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses have an equitable chance to compete for subcontracts.

(9) Assurances that the offeror will include in all subcontracts the contract clause "Utilization of Small Business Concerns." Assure that all subcontractors, other than small businesses, in excess of $500,000 adopt a plan similar to the plan agreed upon by the offeror.

(10) Assurances that the offeror (and any required subcontractors) will cooperate in studies or surveys as required and submit required reports (SF 294 and SF 295) to the Government.

(11) List the types of records the offeror will maintain to demonstrate procedures that have been adopted to comply with the requirement and goals in the plan, including establishing source lists. Also, the offeror shall describe its efforts to locate Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses and award subcontracts to them.

For additional information about each of the above elements required to be contained the subcontracting plan, see FAR Clause 52.219-9, Small Business Subcontracting Plan, and the Sample Subcontracting Plan which is provided as an attachment to this RFP in SECTION J.

(13) **HUBZone Small Business Concerns**

Small Business offerors located in underutilized business zones, called "HUBZones," will be evaluated in accordance with FAR Clause 52.219-4, NOTICE OF PRICE EVALUATION PREFERENCE FOR HUBZONE SMALL BUSINESS CONCERNS, which is incorporated by reference in ARTICLE I.3. of this solicitation. Qualified HUBZone firms are identified in the Small Business Administration website at http://www.sba.gov/hubzone.

(14) **Extent of Small Disadvantaged Business Participation**

In accordance with FAR Subpart 15.304(c)(4), the extent of participation of Small Disadvantaged Business (SDB) concerns in performance of the contract in the authorized NAICS Industry Subsectors shall be evaluated in unrestricted competitive acquisitions expected to exceed $500,000 ($1,000,000 for construction) subject to certain limitations (see FAR 19.1202-1 and 19.1202-2(b). The dollar amounts cited above include any option years/option quantities that may be included in this solicitation. The definition of a "small disadvantaged business" is cited in FAR 19.001.

The factor entitled “Extent of Small Disadvantaged Business Participation” as set forth under the Evaluation Criteria in Section M shall be used for evaluation purposes. Credit under this evaluation factor is not available to SDB concerns that receive a Price Evaluation Adjustment (PEA) under FAR 19.11. Therefore, an SDB will be evaluated on this factor only if that SDB concern waives the PEA. **Waiver of the price evaluation adjustment shall be clearly stated in the proposal.**

The Department of Commerce determines, on an annual basis, by Subsectors, as contained in the North American Industry Classification System (NAICS) codes, and region, if any, the authorized SDB procurement mechanisms and applicable factors (percentages). The NAICS codes can be found at: http://www.sba.gov/size

The Department of Commerce website for the annual determination is:
http://www.arnet.gov/References/sdbadjustments.htm

Offerors shall include with their offers, SDB targets, expressed as dollars and percentages of total contract value, in each of the applicable, authorized NAICS Industry Subsector(s). The applicable authorized NAICS Industry Subsector(s) for this project is (are) identified elsewhere in this RFP. A total target for SDB participation by the prime contractor, that includes any joint ventures and team members, shall be provided as well as a total target for SDB participation by subcontractors. In addition, offerors must provide information that describes their plans for meeting the targets set forth in their proposal. **This information shall be provided in one clearly marked section of the Business Proposal, which shall describe the extent of participation of SDB concerns in the performance of the contract.**

If the evaluation factor in this solicitation includes an SDB evaluation factor or subfactor that considers the extent to which SDB concerns are specifically identified, the SDB concerns considered in the evaluation shall be listed in any resultant contract. Offerors should note that addressing the extent of small disadvantaged business participation **is not in any way intended to be a substitute** for submission of the subcontracting plan, if it is required by this solicitation. An example of the type of information that might be given (in addition to the narrative describing the plan for meeting the targets) follows:

EXAMPLE

Targets for SDB Participation - NAICS Industry Subsector 223

	SDB Percentage of Total Contract Value	SDB Dollars
Total Contract Value- $1,000,000	25%	$250,000
SDB Participation by Prime	10%	$100,000
(Includes joint venture partners and team arrangements)*		
SDB Participation by subcontractors	15%	$150,000

***NOTE:** FAR Subpart 9.6 defines "Contractor team arrangements" to include two or more companies forming a partnership or joint venture to act as a potential prime contractor, or a potential prime contractor who agrees with one or more companies to have them act as its subcontractors on a specific contract or acquisition program. For purposes of evaluation of the SDB participation factor, FAR 19.1202-4 requires that SDB joint ventures and teaming arrangements at the prime level be presented separately from SDB participation by subcontractors.

(15) **Reimbursement of Costs for Independent Research and Development Projects** (Commercial Organizations Only)

The primary purpose of the Public Health Service (PHS) is to support and advance independent research within the scientific community. This support is provided in the form of contracts and grants totaling approximately 7 billion dollars annually. PHS has established effective, time tested and well recognized and accepted procedures for stimulating and supporting this independent research by selecting from multitudes of proposals those research projects most worthy of support within the constraints of its appropriations. The reimbursement of independent research and development costs not incidental to product improvement, through the indirect cost mechanism, would circumvent this competitive process.

To ensure that all research and development projects receive similar and equal consideration, all offerors may compete for direct funding for independent research and development projects they consider worthy of support by submitting those projects to the appropriate Public Health Service grant and/or contract office for review. Since these projects may be submitted for direct funding, the successful offeror agrees that no costs for any independent research and development project, including applicable indirect costs, will be claimed under any contract resulting from this solicitation.

(16) **Salary Rate Limitation in Fiscal Year 2002 ****

Offerors are advised that pursuant to P.L. 107-116, no NIH Fiscal Year 2002 (October 1, 2001 - September 30, 2002) funds may be used to pay the direct annual salary of an individual through any contract awarded as a result of this solicitation at a rate in excess of the Executive Schedule, Level I* (direct salary is exclusive of Overhead, Fringe Benefits and General and Administrative expenses, also referred to as "indirect cost" or "facilities and administrative (F&A) costs"). Direct salary has the same meaning as the term "institutional base salary." An individual's direct salary (or institutional base salary) is the annual compensation that the contractor pays for an individual's appointment whether that individual's time is spent on research, teaching, patient care or other activities. Direct salary (or institutional base salary) excludes any income that an individual may be permitted to earn outside of duties to the contractor.

This does not preclude the offeror from absorbing that portion of an employee's annual salary (plus the dollar amount for fringe benefits and associated indirect costs) that exceeds a rate of the Executive Schedule, Level I*. The salary rate limitation set by P.L. 107-116 applies only to Fiscal Year 2002 funds, however, salary rate ceilings for subsequent years may be included in future DHHS appropriation acts. Multi-year contracts awarded pursuant to this solicitation may be subject to unilateral modifications by the Government if an individual's annual salary exceeds any salary rate ceiling established in future appropriations acts. The Executive Schedule, Level I* annual

salary rate limit also applies to individuals proposed under subcontracts, however it does not apply to consultants. P.L. 107-116 states in pertinent part:

> "None of the funds appropriated in this Act for the National Institutes of Health, the Agency for Healthcare Research and Quality, and the Substance Abuse, and Mental Health Services Administration shall be used to pay the salary of an individual through a grant or extramural mechanism at a rate in excess of Executive Level I."

Information regarding the FY-2002 rate can be found at: http://www.opm.gov/oca/02tables/ex.pdf

It should be noted that a similar public law may be enacted in Fiscal Year 2003, at which time that public law will be incorporated into any resultant contract(s).

(17) **Institutional Responsibility Regarding Conflicting Interests of Investigators**

EACH INSTITUTION MUST:

(a) Maintain an appropriate written, enforced policy on conflict of interest that complies with 42 CFR Part 50 Subpart F and/or 45 CFR Part 94 as appropriate and inform each investigator of the Institution's policy, the Investigator's reporting responsibilities, and the applicable regulations. If the Institution carries out the NIH funded research through subgrantees, contractors or collaborators, the Institution must take reasonable steps to ensure that Investigators working for such entities comply with the regulations, either by requiring those investigators to comply with the Institution's policy or by requiring the entities to provide assurances to the Institution that will enable the Institution to comply with the regulations.

(b) Designate an Institutional official(s) to solicit and review financial disclosure statements from each Investigator who is planning to participate in NIH-funded research.

(c) Require that by the time an application/proposal is submitted to the NIH each investigator who is planning to participate in the NIH-funded research has submitted to the designated official(s) a listing of his/her known Significant Financial Interests (and those of his/her spouse and dependent children): (i) that would reasonably appear to be affected by the research for which the NIH funding is sought; and (ii) in entities whose financial interests would reasonably appear to be affected by the research. All financial disclosures must be updated during the period of the award, either on an annual basis or as new reportable Significant Financial Interests are obtained.

(d) Provide guidelines consistent with the regulations for the designated official(s) to identify conflicting interests and take such actions as necessary to ensure that such conflicting interests will be managed, reduced, or eliminated.

(e) Maintain records, identifiable to each award, of all financial disclosures and all actions taken by the institution with respect to each conflicting interest for: (1) in the case of grants, at least three years from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 CFR Part 74.53(b) and (2) in the case of contracts, 3 years after final payment or, where applicable, for the other time period specified in 48 CFR Part 4 Subpart 4.7, Contract Records Retention.

(f) Establish adequate enforcement mechanisms and provide for sanctions where appropriate.

(g) Certify, in each application/proposal for funding to which the regulations applies, that:

1) there is in effect at the Institution a written and enforced administrative process to identify and manage, reduce or eliminate conflicting interests with respect to all research projects for which funding is sought from the NIH;

2) prior to the Institution's expenditure of any funds under the award, the Institution will report to the awarding component the existence of a conflicting interest (but not the nature of the interest or other details) found by the Institution and assure that the interest has been managed, reduced or eliminated in accord with the regulations; and for any interest that the Institution identifies as conflicting subsequent to

the expenditure of funds after award, the report will be made and the conflicting interest managed, reduced, or eliminated, at least on a temporary basis within sixty days of that identification;

3) the Institution agrees to make information available, upon request, to the awarding component regarding all conflicting interests identified by the Institution and how those interested have been managed, reduced, or eliminated to protect the research from bias; and

4) the Institution will otherwise comply with the regulations.

(18) **INSTITUTIONAL MANAGEMENT OF CONFLICTING INTERESTS**

(a) The designated official(s) must: (1) review all financial disclosures; and (2) determine whether conflict of interest exists, and if so, determine what actions should be taken by the Institution to manage, reduce or eliminate such conflict of interest. **A conflict of interest exists when the designated official(s) reasonably determines that a Significant Financial Interest could directly and significantly affect the design, conduct, or reporting of the NIH-funded research**.

Examples of conditions or restrictions that might be imposed to manage actual or potential conflicts of interests include, but are not limited to:

(i) public disclosure of significant financial interests;
(ii) monitoring of research by independent reviewers;
(iii) modification of the research plan;
(iv) disqualification of the Investigator(s) from participation in all or a portion of the research funded by the awarding component;
(v) divestiture of significant financial interests; or
(vi) severance of relationships that create actual or potential conflicts of interests.

(b) An Institution may require the management of other conflicting financial interests in addition to those described in paragraph (a) of this section, as the Institution deems appropriate.

(19) **ROTC Access and Federal Military Recruiting on Campus**

Section 514 of the FY 1997 Appropriations Act prohibits NIH from providing contract funds to educational institutions that the Secretary of Defense determines have a policy or practice (regardless of when implemented) that either prohibits, or in effect prevents (1) the maintaining, establishing, or operation of a unit of the Senior Reserve Officer Training Corps at the covered education entity; or (2) a student at the covered educational entity from enrolling in a unit of the Senior Reserve Officer Training Corps at another institution of higher education.

Further, contract funds may not be provided to educational institutions that have a policy or practice that prohibits or prevents (1) entry to campuses, or access to students (who are 17 years of age or older) on campuses, for purposes of Federal military recruiting; or (2) access by military recruiters for purposes of Federal military recruiting to information pertaining to students (who are 17 years of age or older) enrolled at the covered educational entity.

Electronic and Information Technology Accessibility

Section 508 of the Rehabilitation Act of 1973 (29 U.S.C. 794d), as amended by P.L.105-220 under Title IV (Rehabilitation Act Amendments of 1998) and the Architectural and Transportation Barriers Compliance Board Electronic and Information Technology (EIT) Accessibility Standards (36 CFR part 1194) require that all EIT acquired must ensure that:

1. Federal employees with disabilities have access to and use of information and data that is comparable to the access and use by Federal employees who are not individuals with disabilities; and

2. Members of the public with disabilities seeking information or services from an agency have access to and use of information and data that is comparable to the access to and use of information and data by members of the public who are not individuals with disabilities.

This requirement includes the development, maintenance, and/or use of EIT products/services, therefore, any proposal submitted in response to this solicitation must demonstrate compliance with the established EIT Accessibility Standards.

Further information about Section 508 is available via the Internet at http://www.section508.gov .

(20) **Solicitation Provisions Incorporated by Reference**, FAR 52.252-1 (February 1998)

This Solicitation incorporates one or more solicitation provisions by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. The offeror is cautioned that the listed provisions may include blocks that must be completed by the offeror and submitted with its quotation or offer. In lieu of submitting the full text provisions, the offeror may identify the provision by paragraph identifier and provide the appropriate information with its quotation or offer. Also, the full text of a solicitation provision may be accessed electronically at this address: http://www.arnet.gov/far/.

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1):

a) Submission of Offers in the English Language, FAR Clause 52.214-34, (April 1991).

b) Submission of Offers in U.S. Currency, FAR Clause 52.214-35, (April 1991).

c) Facilities Capital Cost of Money, FAR Clause 52.215-16, (October 1997).

d) Order of Precedence-Uniform Contract Format, FAR Clause 52.215-8, (October 1997).

e) Preaward On-Site Equal Opportunity Compliance Evaluation, (Over $10,000,000), FAR Clause 52.222-24, (February 1999).

TECHNICAL PROPOSAL INSTRUCTIONS

A detailed work plan must be submitted indicating how each aspect of the statement of work is to be accomplished. Your technical approach should be in as much detail as you consider necessary to fully explain your proposed technical approach or method. The technical proposal should reflect a clear understanding of the nature of the work being undertaken. The technical proposal must include information on how the project is to be organized, staffed, and managed. Information should be provided which will demonstrate your understanding and management of important events or tasks.

(1) **Technical Discussions**

The technical discussion included in the technical proposal should respond to the items set forth below:

a) **Statement of Work**

(1) Objectives

State the overall objectives and the specific accomplishments you hope to achieve. Indicate the rationale for your plan, and relation to comparable work in progress elsewhere. Review pertinent work already published which is relevant to this project and your proposed approach. This should support the scope of the project as you perceive it.

(2) Approach

Use as many subparagraphs, appropriately titled, as needed to clearly outline the general plan of work. Discuss phasing of research and, if appropriate, include experimental design and possible or probable outcome of approaches proposed.

(3) Methods

Describe in detail the methodologies you will use for the project, indicating your level of experience with each, areas of anticipated difficulties, and any unusual expenses you anticipate.

(4) Schedule

Provide a schedule for completion of the work and delivery of items specified in the statement of work. Performance or delivery schedules shall be indicated for phases or segments, as applicable, as well as for the overall program. Schedules shall be shown in terms of calendar months from the date of authorization to proceed or, where applicable, from the date of a stated event, as for example, receipt of a required approval by the Contracting Officer. Unless the request for proposal indicates that the stipulated schedules are mandatory, they shall be treated as desired or recommended schedules. In this event, proposals based upon the offeror's best alternative schedule, involving no overtime, extra shift or other premium, will be accepted for consideration.

b) **Personnel**

Describe the experience and qualifications of personnel who will be assigned for direct work on this program. Information is required which will show the composition of the task or work group, its general qualifications, and recent experience with similar equipment or programs. Special mention shall be made of direct technical supervisors and key technical personnel, and the approximate percentage of the total time each will be available for this program.

OFFERORS SHOULD ASSURE THAT THE PRINCIPAL INVESTIGATOR, AND ALL OTHER PERSONNEL PROPOSED, SHALL NOT BE COMMITTED ON FEDERAL GRANTS AND CONTRACTS FOR MORE THAN A TOTAL OF 100% OF THEIR TIME. IF THE SITUATION ARISES WHERE IT IS DETERMINED THAT A PROPOSED EMPLOYEE IS COMMITTED FOR MORE THAN 100% OF HIS OR HER TIME, THE GOVERNMENT WILL REQUIRE ACTION ON THE PART OF THE OFFEROR TO CORRECT THE TIME COMMITMENT.

(1) Principal Investigator/Project Director

List the name of the Principal Investigator/Project Director responsible for overall implementation of the contract and key contact for technical aspects of the project. Even though there may be co-investigators, identify the Principal Investigator/Project Director who will be responsible for the overall implementation of any awarded contract. Discuss the qualifications, experience, and accomplishments of the Principal Investigator/Project Director. State the estimated time to be spent on the project, his/her proposed duties, and the areas or phases for which he/she will be responsible.

(2) Other Investigators

List all other investigators/professional personnel who will be participating in the project. Discuss the qualifications, experience, and accomplishments. State the estimated time each will spend on the project, proposed duties on the project, and the areas or phases for which each will be responsible.

(3) Additional Personnel

List names, titles, and proposed duties of additional personnel, if any, who will be required for full-time employment, or on a subcontract or consultant basis. The technical areas, character, and extent of subcontract or consultant activity will be indicated and the anticipated sources will be specified and qualified. For all proposed personnel who are not currently members of the offeror's staff, a letter of commitment or other evidence of availability is required. A resume does not meet this requirement. Commitment letters for use of consultants and other personnel to be hired must include:

- The specific items or expertise they will provide.
- Their availability to the project and the amount of time anticipated.
- Willingness to act as a consultant.
- How rights to publications and patents will be handled.

(4) Resumes

Resumes of all key personnel are required. Each must indicate educational background, recent experience, specific or technical accomplishments, and a listing of relevant publications.

(2) **Technical Evaluation**

Proposals will be technically evaluated in accordance with the factors, weights, and order of relative importance as described in the Technical Evaluation Criteria (SEE SECTION M).

(3) **Additional Technical Proposal Information**

a) Proposals which merely offer to conduct a program in accordance with the requirements of the Government's scope of work will not be eligible for award. The offeror must submit an explanation of the proposed technical approach in conjunction with the tasks to be performed in achieving the project objectives.

b) The technical evaluation is conducted in accordance with the weighted technical evaluation criteria by an initial review panel. This evaluation produces a numerical score (points) which is based upon the information contained in the offeror's proposal only.

(4) **Other Considerations**

Record and discuss specific factors not included elsewhere which support your proposal. Using specifically titled subparagraphs, items may include:

a) Any agreements and/or arrangements with subcontractor(s). Provide as much detail as necessary to explain how the statement of work will be accomplished within this working relationship.

b) Unique arrangements, equipment, etc., which none or very few organizations are likely to have which is advantageous for effective implementation of this project.

c) Equipment and unusual operating procedures established to protect personnel from hazards associated with this project.

d) Other factors you feel are important and support your proposed research.

e) Recommendations for changing reporting requirements if such changes would be more compatible with the offeror's proposed schedules.

(5) **Information Technology Systems Security**

If this project involves Information Technology, the proposal must present a detailed outline of its proposed Information Technology systems security program which complies with the requirements of the Statement of Work, the Computer Security Act of 1987 Office of Management and Budget (OMB) Circular A-130, Appendix III, "Security of Federal Automated Information Systems," and the DHHS Automated Information Systems Security Program Handbook (Release 2.0, dated May, 1994). The proposal will also need to include similar information for any subcontract proposed.

NOTE: OMB A-130 is accessible via web site: http://www.whitehouse.gov/WH/EOP/OMB/html/circular.html

BUSINESS PROPOSAL INSTRUCTIONS

(1) Basic Cost/Price Information

The business proposal must contain sufficient information to allow the Government to perform a basic analysis of the proposed cost or price of the work. This information shall include the amounts of the basic elements of the proposed cost or price. These elements will include, as applicable, direct labor, fringe benefits, travel, materials, subcontracts, purchased parts, shipping, indirect costs and rate, fee, and profit.

(2) Proposal Cover Sheet

The following information shall be provided on the first page of your pricing proposal:

1. Solicitation, contract, and/or modification number;
2. Name and address of Offeror;
3. Name and telephone number of point of contact;
4. Name, address, and telephone number of Contract Administration Office, (if available);
5. Name, address, and telephone number of Audit Office (if available);
6. Proposed cost and/or price; profit or fee (as applicable); and total;
7. The following statement: By submitting this proposal, the offeror, if selected for discussions, grants the contracting officer or an authorized representative the right to examine, at any time before award, any of those books, records, documents, or other records directly pertinent to the information requested or submitted.
8. Date of submission; and
9. Name, title and signature of authorized representative.

This cover sheet information is for use by offerors to submit information to the Government when cost or pricing data are not required but information to help establish price reasonableness or cost realism is necessary. Such information is not considered cost or pricing data, and shall not be certified in accordance with FAR 15.406-2.

(3) Cost and Pricing Data

1. **General Instructions**

A. You must provide the following information on the first page of your pricing proposal:

(1) Solicitation, contract, and/or modification number;
(2) Name and address of offeror;
(3) Name and telephone number of point of contact;
(4) Name of contract administration office (if available);
(5) Type of contract action (that is, new contract, change order, price revision/redetermination, letter contract, unpriced order, or other);
(6) Proposed cost; profit or fee; and total;
(7) Whether you will require the use of Government property in the performance of the contract, and, if so, what property;
(8) Whether your organization is subject to cost accounting standards; whether your organization has submitted a CASB Disclosure Statement, and if it has been determined adequate; whether you have been notified that you are or may be in noncompliance with your Disclosure Statement or CAS, and, if yes, an explanation; whether any aspect of this proposal is inconsistent with your disclosed practices or applicable CAS, and, if so, an explanation; and whether the proposal is consistent with your established estimating and accounting principles and procedures and FAR Part 31, Cost Principles, and, if not, an explanation;
(9) The following statement: This proposal reflects our estimates and/or actual costs as of this date and conforms with the instructions in FAR 15.403-5(b)(1) and Table 15-2. By submitting this proposal, we grant the Contracting Officer and authorized representative(s) the right to examine, at any time before award, those records, which include books, documents, accounting procedures and practices, and other data, regardless of type and form or whether such supporting information is specifically referenced or

included in the proposal as the basis for pricing, that will permit an adequate evaluation of the proposed price;
(10) Date of submission; and
(11) Name, title and signature of authorized representative.

B. In submitting your proposal, you must include an index, appropriately referenced, of all the cost or pricing data and information accompanying or identified in the proposal. In addition, you must annotate any future additions and/or revisions, up to the date of agreement on price, or an earlier date agreed upon by the parties, on a supplemental index.

C. As part of the specific information required, you must submit, with your proposal, cost or pricing data (that is, data that are verifiable and factual and otherwise as defined at FAR 15.401). You must clearly identify on your cover sheet that cost or pricing data are included as part of the proposal. In addition, you must submit with your proposal any information reasonably required to explain your estimating process, including--

(1) The judgmental factors applied and the mathematical or other methods used in the estimate, including those used in projecting from known data; and
(2) The nature and amount of any contingencies included in the proposed price.

D. You must show the relationship between contract line item prices and the total contract price. You must attach cost-element breakdowns for each proposed line item, using the appropriate format prescribed in the "Formats for Submission of Line Item Summaries" section of this table. You must furnish supporting breakdowns for each cost element, consistent with your cost accounting system.

E. When more than one contract line item is proposed, you must also provide summary total amounts covering all line items for each element of cost.

F. Whenever you have incurred costs for work performed before submission of a proposal, you must identify those costs in your cost/price proposal.

G. If you have reached an agreement with Government representatives on use of forward pricing rates/factors, identify the agreement, include a copy, and describe its nature.

H. As soon as practicable after final agreement on price or an earlier date agreed to by the parties, but before the award resulting from the proposal, you must, under the conditions stated in FAR 15.406-2, submit a Certificate of Current Cost or Pricing Data.

(4) **Cost Elements**

Depending on your system, you must provide breakdowns for the following basic cost elements, as applicable:

A. **Materials and services**. Provide a consolidated priced summary of individual material quantities included in the various tasks, orders, or contract line items being proposed and the basis for pricing (vendor quotes, invoice prices, etc.). Include raw materials, parts, components, assemblies, and services to be produced or performed by others. For all items proposed, identify the item and show the source, quantity, and price. Conduct price analyses of all subcontractor proposals. Conduct cost analyses for all subcontracts when cost or pricing data are submitted by the subcontractor. Include these analyses as part of your own cost or pricing data submissions for subcontracts expected to exceed the appropriate threshold in FAR 15.403-4. Submit the subcontractor cost or pricing data as part of your own cost or pricing data as required in paragraph 2.A.(2) of this table. These requirements also apply to all subcontractors if required to submit cost or pricing data.

(1) *Adequate Price Competition*. Provide data showing the degree of competition and the basis for establishing the source and reasonableness of price for those acquisitions (such as subcontracts, purchase orders, material order, etc.) exceeding, or expected to exceed, the appropriate threshold set forth at FAR 15.403-4 priced on the basis of adequate price competition. For interorganizational transfers priced at other than the cost of comparable competitive commercial work of the division, subsidiary, or affiliate of the contractor, explain the pricing method (see FAR 31.205-26(e)).

(2) *All Other*. Obtain cost or pricing data from prospective sources for those acquisitions (such as subcontracts, purchase orders, material order, etc.) exceeding the threshold set forth in FAR 15.403-4 and not otherwise exempt, in accordance with FAR 15.403-1(b) (i.e., adequate price competition, commercial items, prices set by law or regulation or waiver). Also provide data showing the basis for establishing source and reasonableness of price. In addition, provide a summary of your cost analysis and a copy of cost or pricing data submitted by the prospective source in support of each subcontract, or purchase order that is the lower of either $10,000,000 or more, or both more than the pertinent cost or pricing data threshold and more than 10 percent of the prime contractor's proposed price. The Contracting Officer may require you to submit cost or pricing data in support of proposals in lower amounts. Subcontractor cost or pricing data must be accurate, complete and current as of the date of final price agreement, or an earlier date agreed upon by the parties, given on the prime contractor's Certificate of Current Cost or Pricing Data. The prime contractor is responsible for updating a prospective subcontractor's data. For standard commercial items fabricated by the offeror that are generally stocked in inventory, provide a separate cost breakdown, if priced based on cost. For interorganizational transfers priced at cost, provide a separate breakdown of cost elements. Analyze the cost or pricing data and submit the results of your analysis of the prospective source's proposal. When submission of a prospective source's cost or pricing data is required as described in this paragraph, it must be included along with your own cost or pricing data submission, as part of your own cost or pricing data. You must also submit any other cost or pricing data obtained from a subcontractor, either actually or by specific identification, along with the results of any analysis performed on that data.

B. **Direct Labor**. Provide a time-phased (e.g., monthly, quarterly, etc.) breakdown of labor hours, rates, and cost by appropriate category, and furnish bases for estimates.

C. **Indirect Costs**. Indicate how you have computed and applied your indirect costs, including cost breakdowns. Show trends and budgetary data to provide a basis for evaluating the reasonableness of proposed rates. Indicate the rates used and provide an appropriate explanation.

D. **Other Costs**. List all other costs not otherwise included in the categories described above (e.g., special tooling, travel, computer and consultant services, preservation, packaging and packing, spoilage and rework, and Federal excise tax on finished articles) and provide bases for pricing.

E. **Royalties**. If royalties exceed $1,500, you must provide the following information on a separate page for each separate royalty or license fee:

(1) Name and address of licensor.
(2) Date of license agreement.
(3) Patent numbers.
(4) Patent application serial numbers, or other basis on which the royalty is payable.
(5) Brief description (including any part or model numbers of each contract item or component on which the royalty is payable).
(6) Percentage or dollar rate of royalty per unit.
(7) Unit price of contract item.
(8) Number of units.
(9) Total dollar amount of royalties.
(10) If specifically requested by the Contracting Officer, a copy of the current license agreement and identification of applicable claims of specific patents (see FAR 27.204 and 31.205-37).

F. **Facilities Capital Cost of Money**. When you elect to claim facilities capital cost of money as an allowable cost, you must submit Form CASB-CMF and show the calculation of the proposed amount (see FAR 31.205-10).

3. **Formats for Submission of Line Item Summaries**

The detailed breakdown shall be in the format as shown on the form **Breakdown of Proposed Estimated Cost (plus fee) and Labor Hours** (SECTION J, List of Attachments). For each separate cost estimate, the offeror must furnish a breakdown by cost element as indicated above. In addition, summary total amounts shall be furnished. In the event the RFP cites specific line items, by number, a cost breakdown for each line item must be furnished.

To assist in the preparation of future cost estimates, the Projected Consumer Price Index may be accessed at: http://amb.nci.nih.gov/cpi.htm

4. There is a clear distinction between submitting cost or pricing data and merely making available books, records, and other documents without identification. The requirement for submission of cost or pricing data is met when all accurate cost or pricing data reasonably available to the offeror have been submitted, either actually or by specific identification, to the Contracting Officer or an authorized representative. As later information comes into your possession, it should be submitted promptly to the Contracting Officer in a manner that clearly shows how the information relates to the offeror's price proposal. The requirement for submission of cost or pricing data continues up to the time of agreement on price, or an earlier date agreed upon between the parties if applicable.

5. By submitting your proposal, you grant the Contracting Officer or an authorized representative the right to examine records that formed the basis for the pricing proposal. That examination can take place at any time before award. It may include those books, records, documents, and other types of factual information (regardless of form or whether the information is specifically referenced or included in the proposal as the basis for pricing) that will permit an adequate evaluation of the proposed price.

(5) **Total Compensation Plan - Evaluation**

a) **Total Compensation Plan (Professional Employees)**

In establishing compensation levels for professional employees, the total compensation (both salaries and fringe benefits) proposed shall reflect a clear understanding of the requirements of the work to be accomplished and the suitability of the proposed compensation structure to obtain and retain qualified personnel to meet mission objectives. The salary rates or ranges must recognize the distinct differences in professional skills and the complexity of varied disciplines as well as job difficulty. Proposals offering total compensation levels less than currently being paid by the predecessor Contractor for the same work will be evaluated, in addition to the above, on the basis of maintaining program continuity, uninterrupted work of high quality, and availability of required competent professional employees. Offerors are cautioned that instances of lowered compensation for essentially the same professional work may be considered a lack of sound management judgment in addition to indicating a lack of understanding of the requirement.

b) **Cost (Professional Compensation)**

Proposals which are unrealistically low or do not reflect a reasonable relationship of compensation to the professional job categories so as to impair the Contractor's ability to recruit and retain competent professional employees, may be viewed as reflecting a failure to comprehend the complexity of the contract requirements. The Government is concerned with the quality and stability of the work force to be employed on this contract. The compensation data required will be used in evaluation of the offeror's understanding of the contract requirements.

c) **Other (Labor Relations)**

An assessment of the potential for adverse effect upon performance and maintenance of the required number of professional employees with requisite skills resulting from an unrealistically low compensation structure will also be made.

d) **Federal Acquisition Regulation Clauses incorporated by Reference**

FAR Clause 52.222-46, Evaluation of Compensation for Professional Employees (FEBRUARY 1993).

(6) **Qualifications of the Offeror**

You are requested to submit a summary of your "General Experience, Organizational Experience Related to this RFP, Performance History and Pertinent Contracts."

a) **General Experience**

General experience is defined as general background, experience and qualifications of the offeror. A discussion of proposed facilities which can be devoted to the project may be appropriate.

b) **Organizational Experience Related to the RFP**

Organizational experience is defined as the accomplishment of work, either past or on-going, which is comparable or related to the effort required by this RFP. This includes overall offeror or corporate experience, **but not** the experience and/or past performance of individuals who are proposed as personnel involved with the Statement of Work in this RFP.

c) **Performance History**

Performance history is defined as meeting contract objectives within **delivery** and **cost schedules** on efforts, either past or on-going, which is comparable or related to the effort required by this RFP.

d) **Pertinent Contracts**

Pertinent contracts is defined as a listing of each related contract completed within the last three years or currently in process. The listing should include: 1) the contract number; 2) contracting agency; 3) contract dollar value; 4) dates contract began and ended (or ends); 5) description of contract work; 6) explanation of relevance of work to this RFP; 7) actual delivery and cost performance versus delivery and cost agreed to in the contract(s). For award fee contracts, separately state in dollars the base fee and award fee available and the award fee actually received. The same type of organizational experience and past performance data should be submitted.

e) **Pertinent Grants**

List grants supported by the Government that involved similar or related work to that called for in this RFP. Include the grant number, involved agency, names of the grant specialist and the Science Administrator, identification of the work, and when performed.

You are cautioned that omission or an inadequate or inaccurate response to this very important RFP requirement could have a negative effect on the overall selection process. Experience and past performance are factors which are relevant to the ability of the offerors to perform and are considered in the source selection process.

(7) **Other Administrative Data**

e) **Property**

(1) It is DHHS policy that Contractors will provide all equipment and facilities necessary for performance of contracts. Exception may be granted to furnish Government-owned property, or to authorize purchase with contract funds, only when approved by the Contracting Officer. If the offeror is proposing that the Government provide any equipment, other than that specified under Government Furnished Property in the RFP, the proposal must include comprehensive justification which includes:

(a) An explanation that the item is for a special use essential to the direct performance of the contract and the item will be used exclusively for the purpose. Office equipment such as desks, office machines, etc., will not be provided under a contract except under very exceptional circumstances.

(b) No practical or economical alternative exists (e.g., rental, capital investment) that can be used to perform the work.

(2) The offeror shall identify Government-owned property in its possession and/or Contractor titled property acquired from Federal funds, which it proposes to use in the performance of the prospective contract.

(3) The management and control of any Government property shall be in accordance with DHHS Publication (OS) 686 entitled, "Contractors Guide for Control of Government Property (1990)," a copy of which will be provided upon request.

f) **Submission of Electronic Funds Transfer Information with Offer, FAR Clause 52.232-38** (MAY 1999)

The offeror shall provide, with its offer, the following information that is required to make payment by electronic funds transfer (EFT) under any contract that results from this solicitation. This submission satisfies the requirement to provide EFT information under paragraphs (b)(1) and (j) of the clause at 52.232-34, Payment by Electronic Funds Transfer--Other than Central Contractor Registration.

(1) The solicitation number (or other procurement identification number).
(2) The offeror's name and remittance address, as stated in the offer.
(3) The signature (manual or electronic, as appropriate), title, and telephone number of the offeror's official authorized to provide this information.
(4) The name, address, and 9-digit Routing Transit Number of the offeror's financial agent.
(5) The offeror's account number and the type of account (checking, savings, or lockbox).
(6) If applicable, the Fedwire Transfer System telegraphic abbreviation of the offeror's financial agent.
(7) If applicable, the offeror shall also provide the name, address, telegraphic abbreviation, and 9-digit Routing Transit Number of the correspondent financial institution receiving the wire transfer payment if the offeror's financial agent is not directly on-line to the Fedwire and, therefore, not the receiver of the wire transfer payment.

g) **Financial Capacity**

The offeror shall indicate if it has the necessary financial capacity, working capital, and other resources to perform the contract without assistance from any outside source. If not, indicate the amount required and the anticipated source.

h) **Incremental Funding**

An incrementally funded cost-reimbursement contract is a contract in which the total work effort is to be performed over a multiple year period and funds are allotted, as they become available, to cover discernible phases or increments of performance. The incremental funding technique allows for contracts to be awarded for periods in excess of one year even though the total estimated amount of funds expected to be obligated for the contract are not available at the time of the contract award. If this requirement is specified elsewhere in this RFP, the offeror shall submit a cost proposal for each year. In addition, the following provisions are applicable:

i) **HHSAR 352.232-75, Incremental Funding (January 2001)**

(a) It is the Government's intention to negotiate and award a contract using the incremental funding concepts described in the clause entitled Limitation of Funds. Under the clause, which will be included in the resultant contract, initial funds will be obligated under the contract to cover the first year of performance. Additional funds are intended to be allotted to the contract by contract modification, up to and including the full estimated cost of the contract, to accomplish the entire project. While it is the Government's intention to progressively fund this contract over the entire period of performance up to and including the full estimated cost, the Government will not be obligated to reimburse the Contractor for costs incurred in excess of the periodic allotments, nor will the Contractor be obligated to perform in excess of the amount allotted.

(b) The Limitation of Funds clause to be included in the resultant contract shall supersede the Limitation of Cost clause found in the General Provisions.

(End of provision)

j) **Facilities Capital Cost of Money, FAR 52.215-16, (October 1997)**

(This is applicable if you are a commercial organization.)

(a) Facilities capital cost of money [(see FAR 15.408(h)] will be an allowable cost under the contemplated contract, if the criteria for allowability in subparagraph 31.205-10(a)(2) of the Federal Acquisition Regulation are met. One of the allowability criteria requires the prospective Contractor to propose facilities capital cost of money in its offer.

(b) If the prospective Contractor does not propose this cost, the resulting contract will include the clause Waiver of Facilities Capital Cost of Money.

(End of Provision)

If the offeror elects to claim this cost, the offeror shall specifically identify or propose it in the cost proposal for the contract by checking the appropriate box below.

[ ] The prospective Contractor has specifically identified or proposed facilities capital cost of money in its cost proposal and elects to claim this cost as an allowable cost under the contract. Submit Form CASB-CMF (see FAR 31.205-10).

[ ] The prospective Contractor has not specifically identified or proposed facilities capital cost of money in its proposal and elects not to claim it as an allowable cost under the contract.

(8) **Subcontractors**

If subcontractors are proposed, please include a commitment letter from the subcontractor detailing:

a) Willingness to perform as a subcontractor for specific duties (list duties).

b) What priority the work will be given and how it will relate to other work.

c) The amount of time and facilities available to this project.

d) Information on their cognizant field audit offices.

e) How rights to publications and patents are to be handled.

f) A complete cost proposal in the same format as the offeror's cost proposal.

Note: Organizations that plan to enter into a subcontract with an educational concern under a contract awarded under this RFP should refer to the following Web Site for a listing of clauses that are required to be incorporated in Research & Development (R&D) subcontracts with educational institutions:

http://ocm.od.nih.gov/contracts/rfps/FDP/PDPclausecover.htm

(9) **Proposer's Annual Financial Report**

A copy of the organization's most recent annual report must be submitted as part of the business proposal.

(10) **Representations and Certifications**

One copy of the Representations and Certifications attached as Section K shall be completed and be signed by an official authorized to bind your organization. Additionally, a completed copy of the Representations and Certifications shall be submitted from any proposed subcontractor.

(11) **Travel Costs/Travel Policy**

a) **Travel Costs - Commercial**

Costs for lodging, meals, and incidental expenses incurred by Contractor personnel shall be considered to be reasonable and allowable to the extent they do not exceed on a daily basis the per diem rates set forth in the Federal Travel Regulations, General Services Administration (GSA). Therefore, if travel costs are applicable and proposed by offerors, please be advised that they shall be calculated using the per diem rate schedule as established by GSA. Reimbursement of travel costs under any contract awarded from this RFP shall be in accordance with FAR 31.205-46.

b) **Travel Policy**

One copy of the offeror's (and any proposed subcontractor's) written travel policy shall be included in the business proposal (original only). If an offeror (or any proposed subcontractor) does not have a written travel policy, the offeror shall so state.

SECTION M - EVALUATION FACTORS FOR AWARD

1. GENERAL

The major evaluation factors for this solicitation include technical, cost/price factors, and Small Disadvantaged Business (SDB) Participation. Although technical factors are of paramount consideration in the award of the contract, cost/price and SDB participation is also important to the overall contract award decision. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. In any case, the Government reserves the right to make an award(s) to that offeror whose proposal provides the best overall value to the Government.

The evaluation will be based on the demonstrated capabilities of the prospective Contractors in relation to the needs of the project as set forth in the RFP. The merits of each proposal will be evaluated carefully. Each proposal must document the feasibility of successful implementation of the requirements of the RFP. Offerors must submit information sufficient to evaluate their proposals based on the detailed criteria listed below.

The technical proposals will receive paramount consideration in the selection of the Contractor for tis acquisition. The evaluation will be based on the demonstrated capabilities of the prospective contractors in relation to the needs of the project as set forth in the RFP. The merit of each proposal will be evaluated carefully, based on responsiveness to the RFP and thoroughness and feasibility of the technical approach taken. Offerors must submit information sufficient to evaluate their proposals based on the detailed criteria listed below. Failure to provide the information required to evaluate the proposal may result in rejection of that proposal without further consideration.

2. **EVALUATION OF OPTIONS**

It is anticipated that any contract(s) awarded from this solicitation will contain option provision(s) and period(s).

In accordance with FAR Clause 52.217-5, Evaluation of Options, (July 1990), the Government will evaluate offers for award purposes by adding the total price for all options to the total price for the basic requirement, except when it is determined in accordance with FAR 17.206(b) not to be in the Government's best interests. Evaluation of options will not obligate the Government to exercise the option(s).

3. **EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION**

SDB participation will not be scored, but the Government's conclusions about overall commitment and realism of the offeror's SDB Participation targets will be used in determining the relative merits of the offeror's proposal and in selecting the offeror whose proposal is considered to offer the best value to the Government.

The extent of the offeror's Small Disadvantaged Business Participation Targets will be evaluated before determination of the competitive range. Evaluation of SDB participation will be assessed based on consideration of the information presented in the offeror's proposal. The Government is seeking to determine whether the offeror has demonstrated a commitment to use SDB concerns for the work that it intends to perform.

Offers will be evaluated on the following sub-factors:

(a) Extent of commitment to use SDB concerns
(b) Realism of the proposal
(c) Extent of participation of SDB concerns in terms of the value of the total acquisition.

4. **TECHNICAL EVALUATION CRITERIA**

The evaluation criteria are used by the technical evaluation committee when reviewing the technical proposals. The criteria below are listed in the order of relative importance with weights assigned for evaluation purposes.

1. **Scientific Rationale and Technical Approach (50 points)**

   a) Strength and merit of the documented ability of the Offeror to design, develop, and implement relational databases containing complex data as well as ability to populate, maintain, and provide security for such databases.

   b) Good software engineering practices including documentation and validation specifications.

   c) Appropriateness and adequacy of procedures for data entry from various sources including established databases, extraction of information from existing literature (i.e. journals and publications), and direct Internet-based or electronic mail submission of information from investigators.

   d) Appropriateness and adequacy of methods for data annotation and management (curation), including development of appropriate ontologies, giving high priority to maintaining the integrity of data included within the database.

   e) Appropriateness and adequacy of data retrieval and viewing strategies (browsing and querying), including query methods that ensure intelligent search parameters.

   f) Appropriateness and adequacy of methods to provide access to existing software tools and algorithms, as well as development of improved tools and algorithms directly or through subcontracts or consultants.

2. **Qualifications and Availability of Proposed Scientific Technical Staff (35 points)**

   (a) Principal Investigator: Documented training, expertise, leadership, and availability of a Principal Investigator with technical and administrative competence to successfully manage a project of comparable size and complexity. It is expected that the Principal Investigator shall have knowledge of immunology related to epitopes and an understanding of bioinformatics necessary for planning and directing the project.

   (b) Scientific and Technical Staff, including subcontractors: Documented training, experience, and availability of the proposed professional, technical, and support staff, and documented capabilities to perform their roles in the proposed studies, with documented expertise in similar projects. The adequacy of the staffing plan for the conduct of the project shall include the level of effort of the professional and technical staff, including subcontractors and consultants committed to the project.

   (c) Organization: Documented expertise and leadership in developing and supporting complex and interdisciplinary programs, especially in the areas of software engineering, database design and development, web site design and maintenance, and integration of these fields with such areas as immunology, microbiology, biochemistry, and computational biology.

3. **Facilities and Resources (15 points)**

   (a) Documented availability and adequacy of facilities equipment, and resources necessary to conduct all phases of the proposed project.

   The Contractor must provide:

      1. A detailed facilities plan, including available equipment

      2. Information regarding ownership/lease of the facility, including its documented availability for the duration of the proposed contract.

   3. A plan for obtaining, adding or deleting facilities and equipment as necessary due to progress during the course of database and software development.

SECTION N – REFERENCE MATERIALS

1. Executive Summary: MHC Peptide Database Planning Meeting

NIH Natcher Conference Center
Bethesda, MD

June 5, 2001

A NIAID-sponsored expert panel[1] of immunologists and bioinformaticists met on June 5, 2001 to advise the NIH on relevant biological and informatics issues for possible development of a Major Histocompatibility Complex (MHC)-peptide database.

Antigen processing of proteins into peptides and their subsequent presentation by binding to MHC class I or class II molecules represent the first steps for antigen-specific immune activation. Research on vaccines, autoimmunity, allergy, transplantation, and basic immunological studies would significantly benefit from a comprehensive MHC-peptide database that includes known immunogenic or MHC-binding peptides, as well as prediction tools to identify novel MHC-binding peptide sequences. Researchers have identified immunogenic peptides for a variety of infectious agents and disease states but much of this information is not readily available to the scientific community. Such information could be collated into a publicly accessible, searchable MHC-peptide database to provide researchers with an extremely valuable resource for the development of novel therapeutics. In addition, statistically based prediction tools could be developed for use with the database to define new peptides as vaccine candidates or therapeutic targets. Although several MHC-peptide databases currently exist, they are each of limited scope and do not conform to uniform standards of data collection, entry, or analysis. Therefore, creation of a centralized, standardized database would greatly facilitate utilization of the growing bank of MHC-peptide information.

The meeting featured three sessions focusing on different aspects of the relevant biology. **Session 1** explored three existing peptide databases and the methods used to define peptide binding to MHC. Peptide loading and MHC-peptide complex formation was discussed in **Session 2**. Finally, **Session 3** included presentations and discussions concentrated on MHC and peptide structure. In each of the three sessions, the bioinformatics and database design experts used their knowledge of database and application design to comment on how to best incorporate the biological information into a highly effective database. The meeting ended with a final discussion that focused on the needs of the scientific community and the following recommendations were made by the expert panel to meet those needs.

- There is a need in the community for a comprehensive central MHC-peptide binding database to provide ready access to basic information and analysis/prediction tools.
- Information from existing databases should be consolidated into one large database.
- The database should include negative as well as positive data, since negative data provide valuable information about peptide binding motifs.
- The database should include peptide-binding information for all known MHC molecules from humans and other species (e.g. rodents, nonhuman primates), with a concerted effort to define peptide-binding motifs for currently under-represented MHC molecules.
- High data quality must be maintained for information incorporated into the database.
- Centralized standards should be developed for peptide binding affinity assays, and information from these assays should be used to improve peptide-binding prediction algorithms and artificial neural networks.
- Current peptide-binding algorithms fall short in accurate prediction of peptide immunogenicity. For example, 1 to 5% of naturally occurring peptides contain post-translational modifications that can dramatically impact T cell activation. The rules that govern these post-translational modifications are currently not well defined. It is very important to include this peptide information in a MHC-peptide database in order to enhance basic knowledge of potential epitopes and to improve or develop novel predictive algorithms for peptide binding and immunogenicity. In addition, collaborations between computational biologists and immunologists should be fostered in order to develop more robust computational tools for predicting peptide binding and immunogenicity.

- Bioinformatics issues to consider in database development and population:
    - Knowledge – the data should be unique and fill in knowledge gaps for the community. First determine how much data needs to be included to make a useful impact in the community.
    - Data acquisition/curation – data should come from the community and operate within the rules of the community, and experts in the field should perform curation.
    - Data archives – keep the original submission data together with depositor updates and correspondence; data should be continually updated.
    - Data standards/annotation/ mining – quality control of the data is critical and should be carefully monitored. Impose uniform standards for data submission, and help the community navigate between new information and relevant background information within the database and to other databases via links.
    - Support – long-term commitment to funding and staffing is required to maintain usefulness to the community. Look to the future for new technologies that would improve the database and predictive tools.

[1] Expert Panel: Drs. Talapady Bhat (National Institute of Standards and Technology {NIST}), Soren Buus (University of Copenhagen), Mike Feolo (National Center for Biotechnology Information {NCBI}), Michael Gilson (University of Maryland Biotechnology Institute, Center for Advanced Research in Biotechnology {CARB}), Wolfgang Helmberg (NCBI), William Hildebrand (University of Oklahoma), Donald Hunt (University of Virginia), Alessandro Sette (Epimmune, Inc.), Lawrence Stern (Massachusetts Institute of Technology), Emil Unanue (Washington University), Gregory Vasquez (NIST), and Jonathan Yewdell (NIAID Division of Intramural Research).

2. Planning Meeting Summary: MHC Peptide Database

Goal

An expert panel[2] of immunologists and bioinformaticists was assembled by NIAID for a Major Histocompatibility Complex (MHC)-peptide database planning meeting on June 5, 2001 at the NIH Natcher Conference Center, Bethesda, MD. The meeting was held in order to advise the NIH on relevant biological and informatics issues for possible development of a MHC-peptide database.

Background

MHC class I and class II molecules are polymorphic proteins found on the surface of antigen presenting cells (APC) that function to present antigenic fragments, termed peptides. T lymphocytes recognize these MHC-peptide complexes via their T cell antigen receptors (TCR) and respond by initiating and regulating immune responses and aiding clearance of foreign or aberrant material. The peptides presented by MHC molecules derive from proteolytic cleavage of foreign or self antigens. The MHC molecule binds peptide in a specialized region and holds it stably for T cell recognition. The three dimensional structures of MHC-peptide complexes show intimate contact between the peptide backbone/side chain amino acids and the variable region amino acids of the MHC molecule. Therefore, each distinct MHC molecule has its own rules for peptide binding, but can bind a large number of peptides derived from foreign or self proteins. Given that there are at least 200 different MHC molecules in the human population, and an enormous number of possible peptides derived from self or foreign proteins, the number of potential peptide-MHC complexes is very large.

Rationale for a Central Database

Peptide generation and subsequent binding to MHC class I or class II molecules represent the first steps for antigen-specific immune activation. Research on vaccines, autoimmunity, allergy, transplantation, and basic immunological studies would significantly benefit from a comprehensive MHC-peptide database that includes all known immunogenic or MHC-binding peptides, as well as prediction tools to identify novel MHC-binding peptide sequences. In order to rationally design a new vaccine, researchers would greatly benefit from the ability to accurately predict peptide generation and MHC binding from a particular pathogen genome or protein sequence. A similar strategy would aid the development of important new cancer vaccine candidates. Basic scientists studying antigen processing and presentation, T cell activation, or the development of new assay reagents would greatly benefit from access to information permitting them to expand and test their model systems. Many future therapies to inhibit organ and tissue transplant rejection, autoimmunity, and allergic reactions depend upon knowledge of antigen specificity, which is currently difficult to predict or test, but which could be enormously enhanced by better information on self and environmental peptide association with MHC molecules. Researchers have identified immunogenic peptides for a variety of infectious agents and disease states but much of this information is not readily available to the scientific community. Such information could be collated into a publicly accessible, searchable MHC-peptide database to provide researchers with an extremely valuable resource for the development of novel therapeutics. In addition, statistically-based prediction tools could be developed for use with the database to define new peptides as vaccine candidates or therapeutic targets. Although several MHC-peptide databases do currently exist, they are each of limited scope and do not conform to uniform standards of data collection, entry, or analysis. Therefore, creation of a centralized, standardized database would greatly facilitate utilization of the growing bank of MHC-peptide information.

Meeting Description

The meeting was divided into three sessions composed of short presentations by biologists and bioinformatics experts, followed by group discussions of the pertinent issues (see attached Agenda). **Session 1** focused on the features of three existing databases, summarized in Table 1.

[2] Expert Panel: Drs. Talapady Bhat (National Institute of Standards and Technology {NIST}), Soren Buus (University of Copenhagen), Mike Feolo (National Center of Biotechnology Information {NCBI}), Michael Gilson (University of Maryland Biotechnology Institute, Center for Advanced Research in Biotechnology {CARB}), Wolfgang Helmberg (NCBI), William Hildebrand (University of Oklahoma), Donald Hunt (University of Virginia), Alessandro Sette (Epimmune, Inc.), Lawrence Stern (Massachusetts Institute of Technology), Emil Unanue (Washington University), Gregory Vasquez (NIST), and Jonathan Yewdell (NIAID Division of Intramural Research).

Table 1: Comparison of three current MHC-peptide databases:

Database Origin	Source of peptides/information	Search capabilities/ database content	Other features
HLA ligand/motif database: William Hildebrand, University of Oklahoma	Published data and/or data from direct submission by investigators (accepts unpublished data from an investigator); includes peptide sequence and MHC binding data; obtains peptide binding information from 24 HLA-A alleles, 46 HLA-B alleles, and 19 HLA-C alleles (96% coverage of human MHC class I)	Five search criteria options: a. defined allele and specificity b. advanced search (more criteria than a) c. search by amino acid pattern d. find/match ligands or motifs in an amino acid sequence e. search for ligand by author's last name	Objective: to catalog all known HLA – bound peptides to improve peptide binding motif criteria 1,800 ligands entered Strictly human HLA class I data to date – no other species Database is currently in β testing, will be freely accessible to scientific community Website: http://hlaligand.ouhsc.edu
Quantitative Peptide Binding Predictions: Soren Buus, University of Copenhagen	Generating a large panel of peptide-MHC binding data to train artificial neural networks (ANN) for identification of low, high and non-binders (hard to identify intermediate binders).	ANN : peptide binding motif searches for various HLA molecules. Has 160-200 artificial neurons for first and second generation predictions (homology reduction) – improves predictability of system Contains a large amount of binding data and adding more (400 ligands to date) – makes ANN more robust	Objective: to develop an integrated web-bases service for peptide predictions (will include individual servers predicting proteasome cleavage, MHC binding, and relevant aspects of antigen processing as these become available) Focused exclusively on human HLA data. Information not yet publicly accessible

ESI (Epitope Identification System): Alessandro Sette, Epimmune Inc.	Peptide binding data generated at Epimmune only: various proteins/infectious agents including HIV, HBV, HCV, malaria, TB, influenza, HPV, p53, proteases, Hu2, etc. Identifies 10^4 peptides per year.	Uses peptide-binding data to improve prediction methods. Data included: protein source, amino acid sequence, binding data, original raw data, peptide super-binding data Includes negative data – very important in determining peptide-binding motifs	Objective: To define rules of peptide binding, in order to better predict immunogenic epitopes for vaccine development. Includes peptide binding information for human, mouse, chimp and macaque. Not currently publicly accessible, just through collaborations with Epimmune, but would like to make more accessible Website: http://www.epimmune.com

Several major points emerged from the general discussion following the database presentations. It was clear that each of the databases is unique and contains complementary information that could be integrated into a single large database. Research generally has focused on identification of peptides that bind to commonly expressed class I MHC molecules; therefore, there is a need to gather information about peptides that bind to more diverse MHC class I molecules and also those that bind MHC class II molecules. In addition, more experimental peptide-binding motif data are needed to improve the predictive powers of both artificial neural networks and peptide binding algorithms. Finally, standards need to be established for peptide binding assays to allow data comparison between different laboratories. To this end, Michael Gilson discussed the BindingDB (http://www.bindingdb.org) database of measured binding affinities and suggested that this database structure might be a useful template for a peptide-binding database.

Session 2 was devoted to *in vivo* antigen processing and presentation pathways for both MHC class I and class II molecules. These pathways are summarized in Table 2. Emil Unanue discussed the issues related to peptide display by MHC class II molecules. MHC class II-bound peptides differ from MHC class I peptides because they group into peptide families containing as many as 40 members per family. The peptide sequence includes both "core" and "flanking" residues and is generally larger than 14 amino acids in length. Family composition makes it difficult to develop predictive algorithms based on peptide "core" sequences, since the flanking sequence length can be highly variable within the same family and the flanking sequences are important contributors to antigen presentation and T cell diversity. Emil Unanue found that single amino acid changes within the peptide-binding groove of a class II MHC molecule can completely change the family of peptides selected by that MHC molecule. Similarly, a recent article from Mary Carrington's laboratory (N Engl. J. Med. 2001, 344:1668-1675) showed that a single amino acid change in a class I MHC molecule enhances the risk of AIDS progression in HIV-infected individuals, presumably by altering the peptide specificity of the class I molecule.

Jonathan Yewdell discussed issues important for rational vaccine design and listed five areas of basic research that need further development: (1) the nature of the APCs that activate different types of naïve T cells, (2) the precise location of antigen presentation within the host, (3) the form of antigen presented (post-translational modifications) (4) the time-course of antigen presentation, and (5) the need for a clearer understanding of the complex biology for processing antigens from different sources (e.g. self, viruses, bacteria, parasites). Further knowledge in these areas will help to define general rules of antigen processing and presentation that can be applied to improve predictive tools for peptide-MHC binding and may help to predict immunogenicity.

The general discussion centered on the current inability to predict the immunogenicity of most peptides. Daniel Douek, NIH Vaccine Research Center, mentioned that predictive methods to determine immune reactivity to HIV using peptides have not been successful. However, Denise Doolan, USN Medical Research Center, has successfully used peptide-based predictive models to identify malaria epitopes recognized by antigen-specific T cells. Emil Unanue showed that high peptide binding affinity to class II molecules does not strictly correlate with enhanced T cell responses. For class I, Jonathan Yewdell presented calculations indicating that the chance of a random peptide being immunogenic is 1/2000 but the odds increase to 1/10 or less for peptides known to bind to MHC class I molecules. Thus, knowledge of peptide-MHC binding

may be more useful for predicting CD8+ T cell activation via class I-peptide complexes than for predicting CD4+ T cell activation by MHC class II-peptide complexes. In addition, a greater effort to define peptide-binding motifs for under-studied MHC molecules as well as more detailed characterizations of T cell responses to various pathogenic and self peptides will aid development of novel tools to predict physiologically relevant immune responses.

Table 2: MHC class I and class II processing events and peptide generation

MHC processing pathway	Nature of peptides generated	Subcelluar location of antigen processing events	Accessory molecules involved in peptide transport and/or loading	Source of antigen	Type of T cell activated (and role of T cell in immunity)
MHC class I	Mostly uniform in size: 8-10 amino acids; no flanking amino acids attached to core peptide; fairly easy to define binding motifs	Proteasome: cytosol and nucleus, and non-proteasomal degradation in cytosol	Calreticulin, tapasin, TAP*-1, TAP-2, calnexin	Mainly endogenous proteins (DRiPs*, etc), though some extracellular (endocytosis and other methods of protein uptake)	CD8+ T cells: cytotoxic activity and cytokine release
MHC class II	Highly variable size: 14-24 amino acids long; peptide made of "core" and "flanking" sequences; flanking sequences are highly variable and are important for peptide immunogenicity	Endosomal/lysosomal compartments: parent proteins enter cell via autophagy, endocytosis, phagocytosis	HLA-DM (human), H-2M (mice), HLA-DO (human); Invariant chain and CLIP*	Vesicular proteins (membrane and secretory); cytosolic proteins, extracellular proteins	CD4+T cells: cytokine release, activation of antigen-presenting cells, help to B cells (antibody production) and CD8+ T cells

*TAP = transporter associated with antigen processing, DRiPs = transporter associated with antigen processing, CLIP = class II–associated invariant chain peptide

Issues related to MHC and peptide structure were discussed in **Session 3**. Lawrence Stern described the three-dimensional structure of the peptide-binding groove of MHC class II molecules. Twenty class II MHC-peptide complex structures have been solved for six MHC alleles, including human HLA DR, DQ, a DQ analog and mouse MHC IA^k. These structures could be used as model templates to predict peptide binding but robust predictive tools are not yet available. Lawrence Stern also stated that, in his experience, the current predictive algorithms designed to define MHC class II-binding peptides are not as useful as MHC class I-peptide binding algorithms for narrowing down potential peptide candidates.

Donald Hunt explained the extraordinary power of mass spectrometry (MS) for determining the amino acid sequence of *in vivo* generated MHC-bound peptides. Surprisingly, one to five percent of MHC-bound peptides on the cell surface exhibit post-translational modifications that would not be predicted from the nucleotide or amino acid sequence of the protein, given current prediction methods. Such modified peptides can be recognized by T cells and might well serve as vaccine or therapeutic candidates. MS technology can detect these modifications and help to define the rules governing the various modification motifs. In addition, MS has surpassed T cell assays in sensitivity for detecting endogenously generated peptides; MS analysis also provides peptide sequence information. One of the greatest strengths of MS is its ability to identify a large proportion of the diverse peptides generated by a particular cell type. This sequence information will help to

answer many basic questions about antigen processing within a cell and may lead to development of more robust predictive algorithms for peptide binding and immunogenicity.

In each of the three sessions, the bioinformatics and database design experts used their knowledge of database and application design to comment on how to best incorporate the biological information into a highly effective database. Some of the critical recommendations are:

- Knowledge – the data should be unique and fill in knowledge gaps for the community. First determine how much data needs to be included to make a useful impact in the community.
- Data acquisition/curation – data should come from the community and operate within the rules of the community, and curation should be performed by experts in the field.
- Data archives – keep the original submission data together with depositor updates and correspondence; data should be continually updated.
- Data standards/annotation/ mining – quality control of the data is critical and should be carefully monitored. Impose uniform standards for data submission, and help the community navigate between new information and relevant background information within the database and to other databases via links.
- Support – long-term commitment to funding and staffing is required to maintain usefulness to the community. Look to the future for new technologies that would improve the database and predictive tools.

Conclusions and recommendations to NIH staff

The meeting ended with a final discussion that focused on the needs of the scientific community and recommendations by the expert panel to meet those needs.

- There is a need in the community for a comprehensive MHC-peptide binding database as a central resource to provide ready access to basic information and analysis/prediction tools. This database should include negative as well as positive data, since negative data provide valuable information about peptide binding motifs.
- Information from existing databases should be consolidated into one large database.
- The database should include peptide-binding information for all known MHC molecules from humans and other species (e.g. rodents, nonhuman primates). There should be a concerted effort to define peptide-binding motifs for MHC molecules currently under-represented in existing databases.
- High data quality must be maintained for information incorporated into the database.
- Centralized standards should be developed for peptide binding affinity assays, and information from these assays should be used to improve peptide-binding prediction algorithms and artificial neural networks.
- 1 to 5% of naturally occurring peptides contain post-translational modifications, some of which occur after antigen processing events, and these modifications can dramatically impact T cell activation. The rules that govern these post-translational modifications are currently not well defined. Therefore, the best way to identify modified peptides is by direct sequence analysis using HPLC and mass spectrometry technologies. It is very important to include this peptide information in a MHC-peptide database in order to enhance basic knowledge of potential epitopes and to improve or develop novel predictive algorithms for peptide binding and immunogenicity.
- Current peptide-binding algorithms fall short in accurate prediction of peptide immunogenicity. Therefore, it is necessary to foster collaborations between computational biologists and immunologists in order to develop more robust computational tools for predicting peptide binding and immunogenicity.